STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 134480

TO: Zohreh Fay **Location: 3a61 / 3c70** **Wednesday, October 13, 2004** **Art Unit: 1614** **Phone: 272-0573** **Serial Number: 10 / 663464**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

SEARCH REQUEST FORM

Access DB# 134480

Scientific and Technical Information Center

Requester's Full Name: Zohreh Fay
Art Unit: 1614 Phone Number #(571) 272-0573 Examiner #: 66646 Date: 10/5/04
Mail Box and Bldg/Room Location: 3C70 Serial Number: 10/663,464
Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. ME

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Method of for delivering drugs To the Retina

Inventors (please provide full names): Campochiaro, Peter; Wang, Michael; Yen, Shan-Fong

Earliest Priority Filing Date: 9/18/02

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the claimed composition and the use thereof.

Jan

STAFF USE ONLY

Searcher: an
Searcher Phone #: 22504
Searcher Location:
Date Searcher Picked Up: 10/13
Date Completed: 10/13
Searcher Prep & Review Time:
Clerical Prep Time: 15
Online Time: +60

PTO-1590 (8-01)

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#) ✓
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

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FILE 'REGISTRY' ENTERED AT 07:05:50 ON 13 OCT 2004
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   11 OCT 2004  HIGHEST RN 760932-70-5
DICTIONARY FILE UPDATES:  11 OCT 2004  HIGHEST RN 760932-70-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L2                STR
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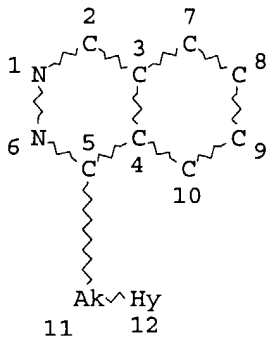


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GGCAT   IS MCY  AT  12
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E5 C  E1 N  AT  12

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
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L5               STR
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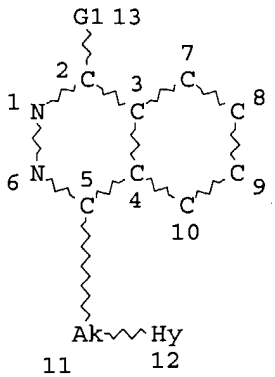


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GGCAT   IS MCY  AT  12
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS E5 C  E1 N  AT  12

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED    548 ITERATIONS                          333 ANSWERS
SEARCH TIME: 00.00.01


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                 SAV L4 FAY663/A
L5               STR L2
L6            18 S L5 CSS SAM SUB=L4
L7           333 S L5 CSS FUL SUB=L4
                 SAV L7 FAY663A/A
L8           325 S L4 NOT L7

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L10            4 S L8
L11            7 S L9,L10
                 SEL AN
                 EDIT /AN /OREF
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L12           11 S E1-E7
                 SEL AN 3 5 9 11
L13            7 S L12 NOT E8-E15
L14          109 S L7
L15           52 S L8
L16          142 S L13-L15
L17            1 S US20040102444/PN OR (US2003-663464# OR YS2002-411669#)/AP,PRN
                 E CAMPOCHIARO P/AU
L18          120 S E3-E7
                 E WONG M/AU
L19          751 S E3-E38
                 E WONG MICHEL/AU
L20           33 S E4-E10
                 E YEN S/AU
L21          112 S E3,E8
L22           22 S E38-E41
                 E PA L17
                 E NOVARTI/PA,CS
L23         4463 S E5,E6 OR NOVARTIS?/PA,CS
L24           29 S L16 AND L17-L23
                 E EYE/CT
L25        64373 S E3-E151
                 E E3+ALL
L26        75310 S E8,E7+NT
                 E E25+ALL
L27        32125 S E8,E9,E7+NT
                 E EYE DISEASE/CT
L28         9912 S E23
L29        24019 S E24-E108
L30         4005 S E109-E115
L31         8855 S E133,E136-E141
                 E EYE+ALL/CT
                 E E26+ALL
L32        12626 S E11,E12,E10+NT
                 E E38+ALL
L33         4225 S E4,E3+NT
L34         1383 S E16+OLD,NT OR E15+OLD,NT
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                 E E27+ALL
L35         3320 S E4,E5,E3+NT OR E10+OLD,NT
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L37       113531 S EYE?
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L39            9 S L24 AND L25-L38
L40            6 S L39 AND ?DIABET?
L41            9 S L39,L40
L42           23 S L16 AND L25-L38
L43           16 S L42 AND ?DIABET?
L44           23 S L42,L43,L41
L45           19 S L44 AND (PD<=20020918 OR PRD<=20020918 OR AD<=20020918)
L46            7 S L45 AND L24
L47           12 S L45 NOT L46
                 SEL DN AN 1 10 11
L48            9 S L47 NOT E1-E9
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L50            4 S L44 NOT L45
L51            1 S L50 AND OCULAR THERAPY
L52           17 S L49,L51
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L57          33 S L54 NOT L55,L56
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L62         108 S L60,L61
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L66          14 S L64,L65 AND ?DIABET?
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L71           1 S L70 AND RETINA
L72           2 S L51,L71
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L78           2 S L77 AND DIABET?/CT
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L80          16 S L77-L79

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FILE COVERS 1907 - 13 Oct 2004  VOL 141 ISS 16
FILE LAST UPDATED: 12 Oct 2004  (20041012/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d l80 all hitstr tot

L80  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:493567  HCAPLUS
DN   141:47380
ED   Entered STN:  18 Jun 2004
TI   Ocular therapy
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IN **Campochiaro, Peter A.**
PA USA
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-502
NCL 514248000
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004116434	A1	20040617	US 2003-704297	20031107
PRAI US 2002-424609P	P	20021107		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004116434	ICM	A61K031-502
	NCL	514248000

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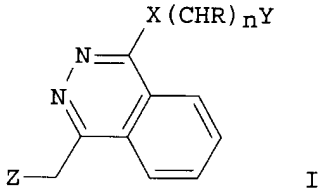


I

AB A method for treating a subject suffering from **epiretinal** membrane formation or **retinal** detachment due to **epiretinal** membrane formation is disclosed. The method comprises administering a compound of the formula I wherein n is 0 to 2, R is H or lower alkyl; X is imino, oxa, or thia; Y is aryl; and Z is unsubstituted or substituted pyridyl, an N-oxide thereof, wherein 1 or more N atoms carry an oxygen atom, or a salt thereof.

ST **retinal** detachment therapy method phthalazine deriv VEGF

IT **Eye, disease**
(**epiretinal** membrane formation; **ocular therapy** with phthalazine derivs.)

IT Human
(**ocular therapy** with phthalazine derivs.)

IT **Eye, disease**
(**retina, detachment; ocular therapy** with phthalazine derivs.)

IT Drug delivery systems
(solns., **ophthalmic; ocular therapy** with phthalazine derivs.)

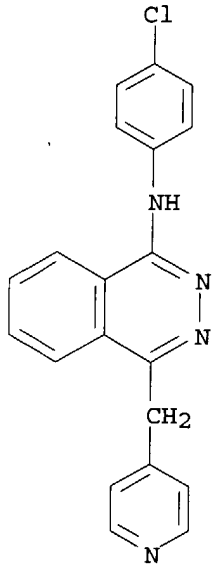
IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ocular therapy** with phthalazine derivs.)

IT 253-52-1D, Phthalazine, derivs. 120685-11-2, N-Benzoyl staurosporine
212141-54-3 212141-57-6 212141-58-7
212141-59-8 212141-60-1 212141-64-5
212141-66-7 212141-67-8 212141-68-9
212141-69-0 212141-70-3 212141-72-5
212141-73-6 212141-74-7 212141-75-8
212141-88-3 212141-91-8 212141-92-9
212142-82-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ocular therapy** with phthalazine derivs.)

IT **212141-54-3 212141-57-6 212141-58-7**
212141-59-8 212141-60-1 212141-64-5
212141-66-7 212141-67-8 212141-68-9
212141-69-0 212141-70-3 212141-72-5
212141-73-6 212141-74-7 212141-75-8
212141-88-3 212141-91-8 212141-92-9
212142-82-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ocular therapy** with phthalazine derivs.)

RN 212141-54-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



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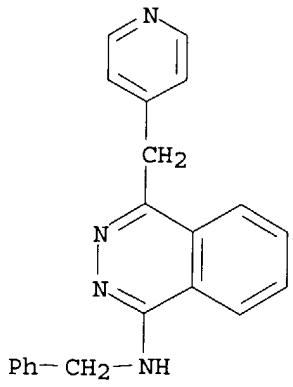

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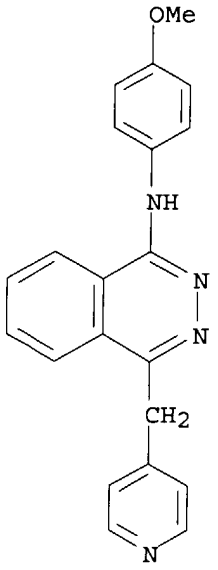
CN 1-Phthalazinamine, N-(4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA

INDEX NAME)



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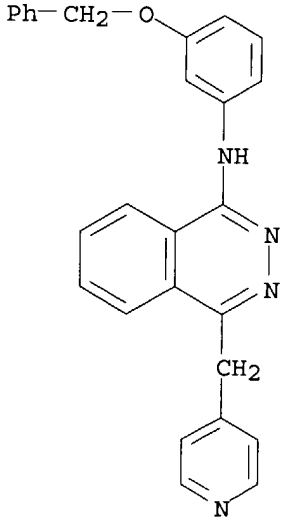

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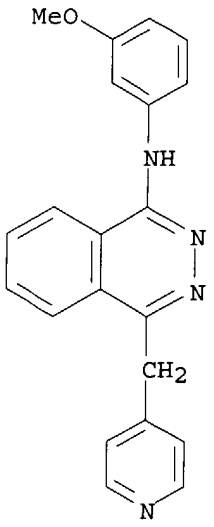

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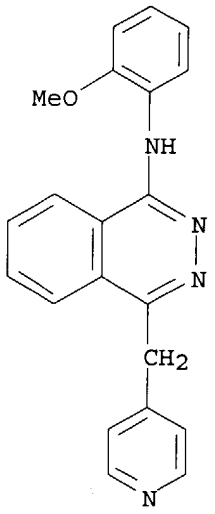

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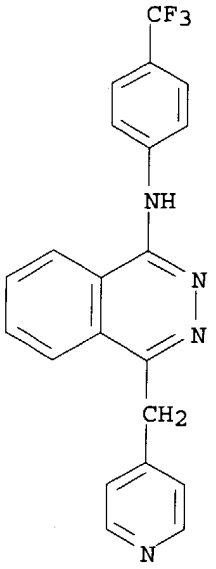

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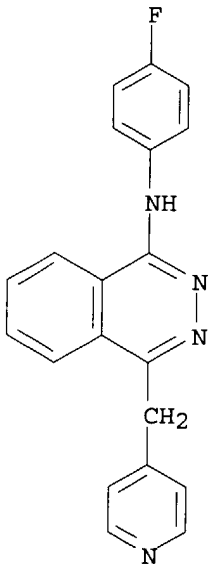

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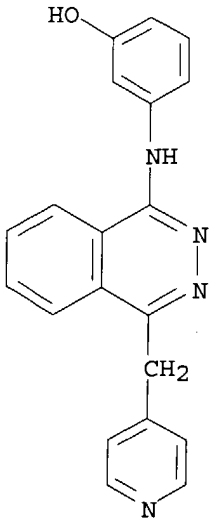

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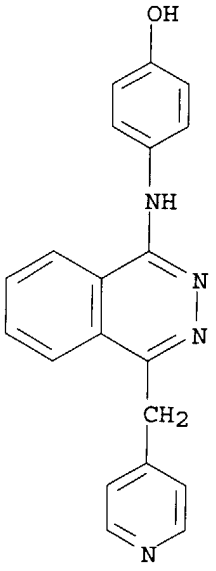

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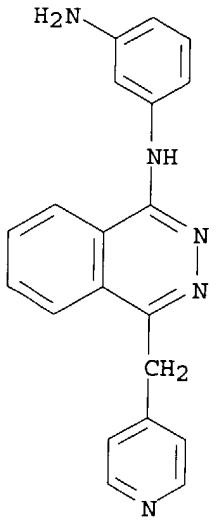

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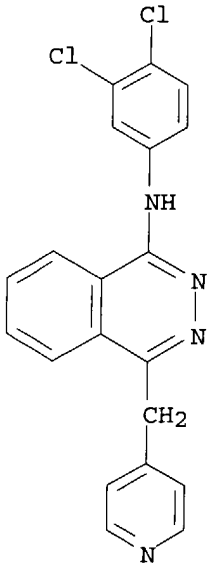

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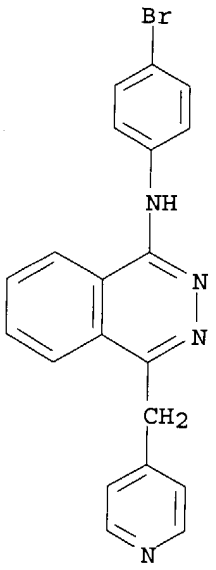

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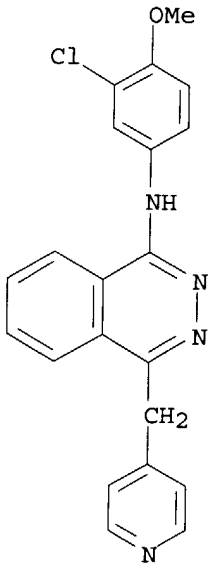

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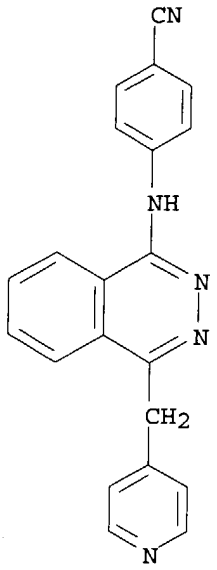

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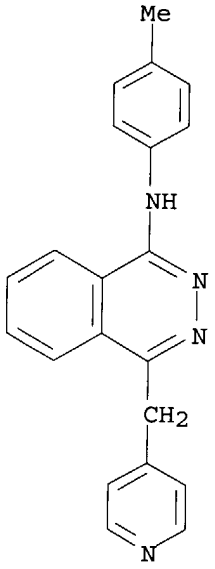

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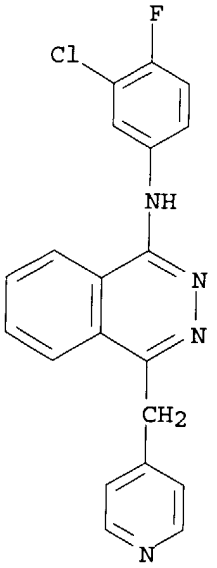

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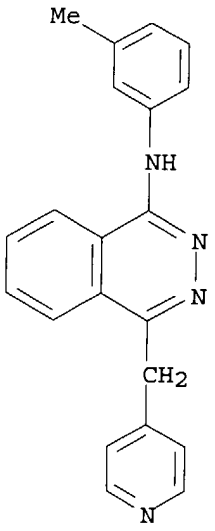

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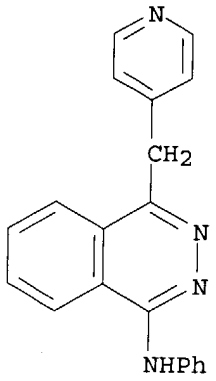

L80 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
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DN 141:12280
ED Entered STN: 28 May 2004
TI Method for delivering phthalazine drugs to the **retina**
IN **Campochiaro, Peter**; **Wong, Michelle**; **Yen, Shau-Fong**
PA USA
SO U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-503
NCL 514248000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 28
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004102444	A1	20040527	US 2003-663464	20030916 <--
PRAI US 2002-411669P	P	20020918 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004102444	ICM	A61K031-503
	NCL	514248000

OS MARPAT 141:12280
AB The invention relates to methods for the delivery of certain phthalazine derivs. to the **retina**(s) of a subject in need of treatment. Thus, a formulation contained **PTK-787** 1.0, Polysorbate-80 0.1, Carbopol-980 NF 0.25, HPMC 0.3, sorbitol 3.43, benzalkonium chloride 0.015, and water qs to 100%.
ST phthalazine drug **retina** prepn
IT **Eye, disease**
(**diabetic retinopathy**, proliferative; method for delivering phthalazine drugs to **retina**)
IT **Eye, disease**
(**macula, degeneration**; method for delivering phthalazine drugs to **retina**)
IT **Eye, disease**
(**macular edema**; method for delivering phthalazine drugs to **retina**)
IT Human
(method for delivering phthalazine drugs to **retina**)
IT **Angiogenesis**

(**neovascularization**, **retinal**; method for delivering phthalazine drugs to **retina**)

IT **Eye, disease**
(**retina**, **neovascularization**; method for delivering phthalazine drugs to **retina**)

IT **Eye**
(**retina**; method for delivering phthalazine drugs to **retina**)

IT **Eye, disease**
(**retinopathy**, ischemic; method for delivering phthalazine drugs to **retina**)

IT Drug delivery systems
(topical; method for delivering phthalazine drugs to **retina**)

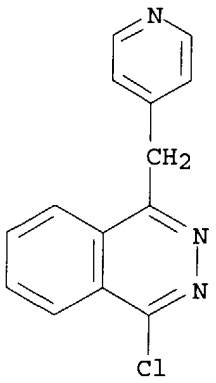
IT 106-47-8, 4-Chloroaniline, reactions 20265-96-7, 4-Chloroaniline hydrochloride **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for delivering phthalazine drugs to **retina**)

IT **212141-51-0P 212141-52-1P 212141-54-3P, PTK 787**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for delivering phthalazine drugs to **retina**)

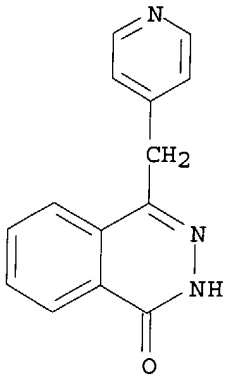
IT **212141-57-6 212141-58-7 212141-59-8 212141-60-1 212141-64-5 212141-66-7 212141-67-8 212141-68-9 212141-69-0 212141-70-3 212141-72-5 212141-73-6 212141-74-7 212141-75-8 212141-88-3 212141-91-8 212141-92-9 212142-82-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for delivering phthalazine drugs to **retina**)

IT **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for delivering phthalazine drugs to **retina**)

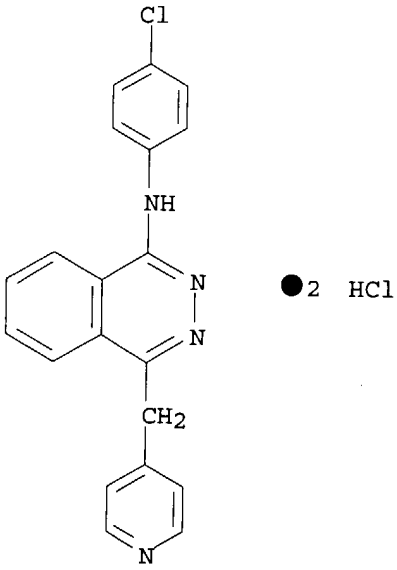
RN 101094-85-3 HCAPLUS
CN Phthalazine, 1-chloro-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



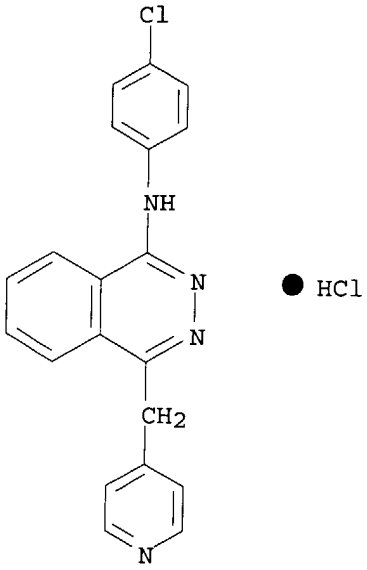
RN 107558-48-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



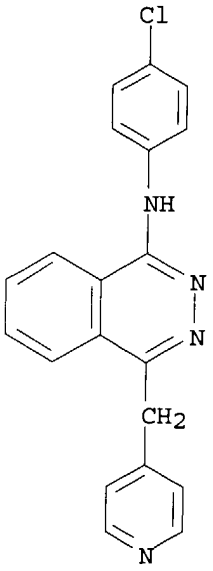
IT **212141-51-0P 212141-52-1P 212141-54-3P, PTK 787**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for delivering phthalazine drugs to **retina**)
RN 212141-51-0 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



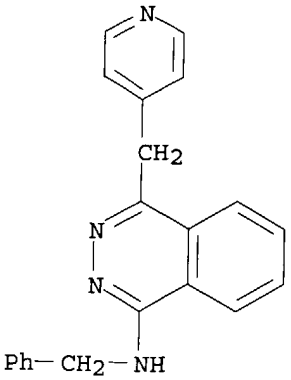
RN 212141-52-1 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



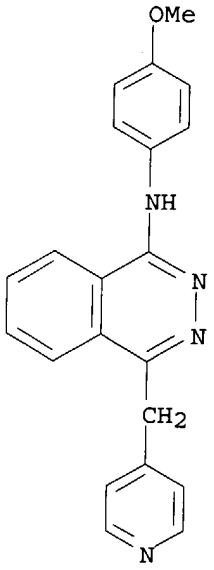
RN 212141-54-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



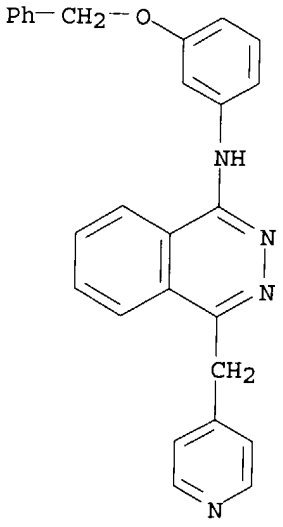
IT **212141-57-6 212141-58-7 212141-59-8**
212141-60-1 212141-64-5 212141-66-7
212141-67-8 212141-68-9 212141-69-0
212141-70-3 212141-72-5 212141-73-6
212141-74-7 212141-75-8 212141-88-3
212141-91-8 212141-92-9 212142-82-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for delivering phthalazine drugs to **retina**)
RN 212141-57-6 HCAPLUS
CN 1-Phthalazinamine, N-(phenylmethyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



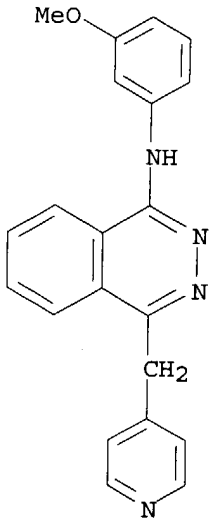
RN 212141-58-7 HCAPLUS
CN 1-Phthalazinamine, N-(4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-59-8 HCAPLUS
CN 1-Phthalazinamine, N-[3-(phenylmethoxy)phenyl]-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-60-1 HCAPLUS
CN 1-Phthalazinamine, N-(3-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-64-5 HCAPLUS
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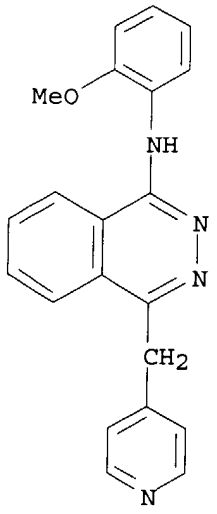
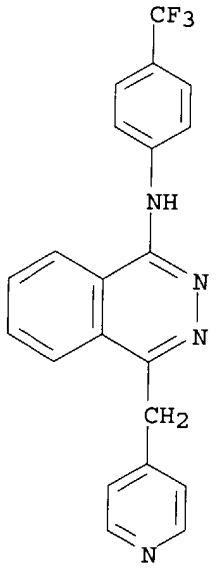
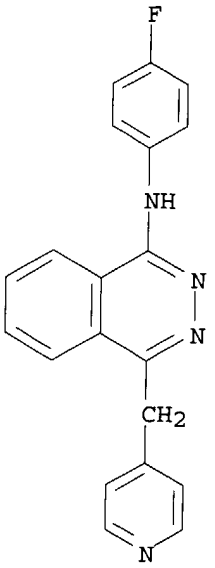


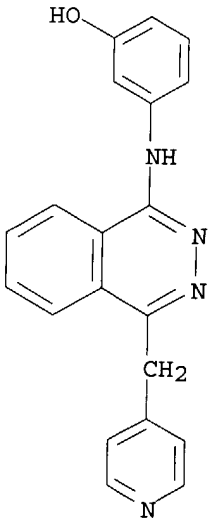
RN 212141-66-7 HCAPLUS
CN 1-Phthalazinamine, 4-(4-pyridinylmethyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



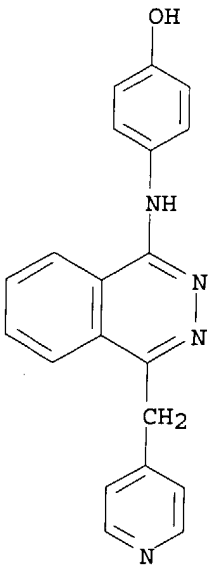
RN 212141-67-8 HCAPLUS
CN 1-Phthalazinamine, N-(4-fluorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-68-9 HCAPLUS
CN Phenol, 3-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



RN 212141-69-0 HCAPLUS
CN Phenol, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



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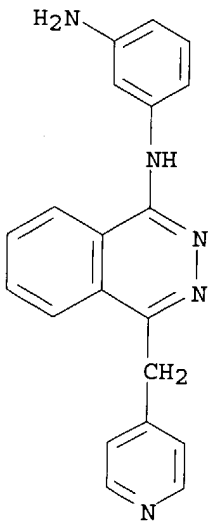

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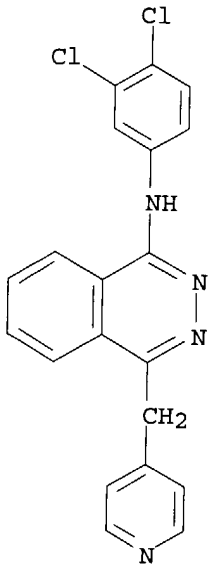
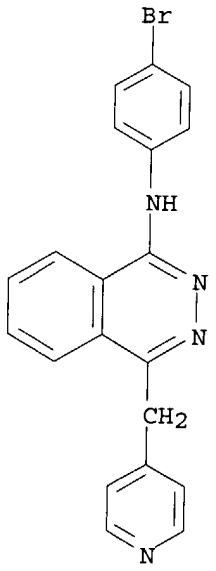
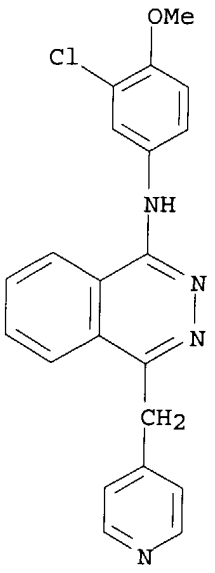
CN 1-Phthalazinamine, N-(3,4-dichlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



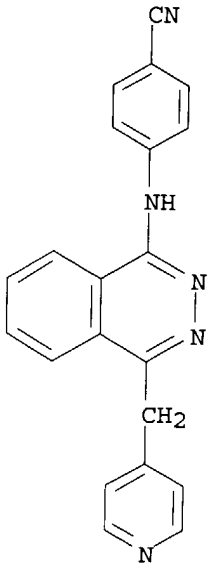
RN 212141-73-6 HCAPLUS
CN 1-Phthalazinamine, N-(4-bromophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



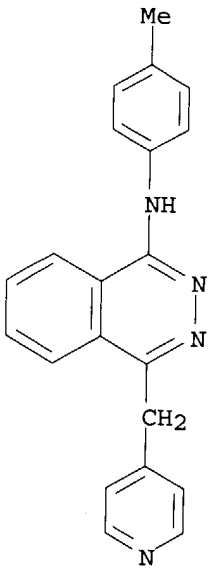
RN 212141-74-7 HCAPLUS
CN 1-Phthalazinamine, N-(3-chloro-4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



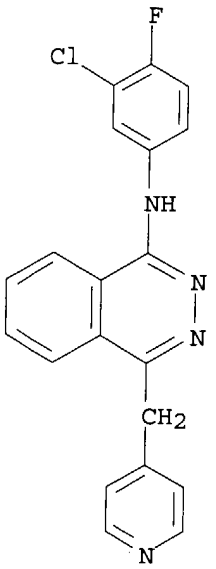
RN 212141-75-8 HCAPLUS
CN Benzonitrile, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



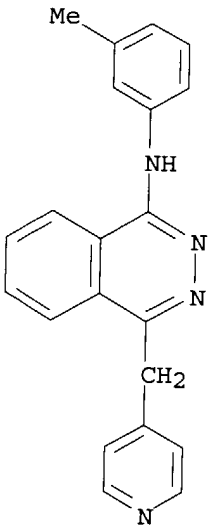
RN 212141-88-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-methylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



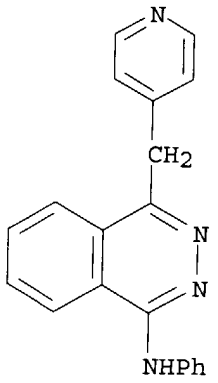
RN 212141-91-8 HCAPLUS
CN 1-Phthalazinamine, N-(3-chloro-4-fluorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-92-9 HCAPLUS
CN 1-Phthalazinamine, N-(3-methylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212142-82-0 HCAPLUS
CN 1-Phthalazinamine, N-phenyl-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80480 HCAPLUS
DN 140:133854
ED Entered STN: 01 Feb 2004
TI **Ophthalmic** ointment composition comprising a drug, an ointment base and a solubilizing/dispersing agent
IN Aukunuru, Jithan; Babiole, Saunier Maggy; Bizec, Jean-claude; Kis, Georg Ludwig; Schoch, Christian; **Wong, Michelle Pik-han**
PA **Novartis Ag, Switz.**; **Novartis Pharma Gmbh**; Babiole Saunier, Maggy
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-06
ICS A61K031-404; A61P027-02
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004009056 A1 20040129 WO 2003-EP8005 20030722 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, ML
PRAI US 2002-397865P P 20020723 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004009056	ICM	A61K009-06
	ICS	A61K031-404; A61P027-02

AB This invention relates to a semisolid **ophthalmic** composition, in particular an ointment, comprising (1) an **ophthalmic** drug, e. g. a staurosporine derivative, (2) an ointment base and (3) an agent for dispersing and/or dissolving said drug in the ointment base, selected from a polyethylene-glycol, a polyethoxylated castor oil, an alc. having 12 to 20 carbon atoms and a mixture of two or more of said components. An **ophthalmic** ointment contained PKC-412 0.5, white petrolatum 60, wool fat 6, liquid paraffin 29.9, PEG-400 3, phenylethyl alc. 0.5, and alpha-tocopherol 0.1%.

ST **ophthalmic** ointment drug solubilizer dispersing agent

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C12-20, ethoxylated; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT **Edema**
(**diabetic macular**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT **Eye, disease**
(**diabetic retinopathy**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT **Eye**
(**lid**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT Paraffin oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

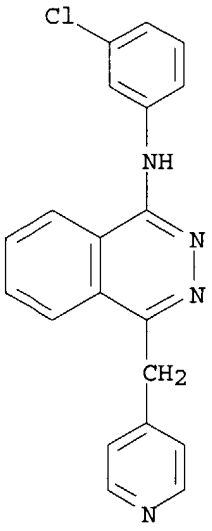
IT **Eye, disease**
(**macula**, **degeneration**, age-related; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT Hydrocarbon waxes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(natural; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)

IT **Angiogenesis**
(**neovascularization**, **eye**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing

dispersing agent)
IT **Eye, disease**
(**neovascularization**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
IT Drug delivery systems
(ointments, **ophthalmic**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
IT Beeswax
Dispersing agents
Eye, disease
Preservatives
Skin
Solubilizers
(**ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
IT Carnauba wax
Hydrocarbon waxes, biological studies
Lanolin
Paraffin waxes, biological studies
Petrolatum
Polyoxyalkylenes, biological studies
Quaternary ammonium compounds, biological studies
Wool wax
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
IT Drug delivery systems
(**ophthalmic**; **ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
IT 58-95-7, α-Tocopherol acetate 59-02-9, α-Tocopherol 60-12-8, Phenyl ethyl alcohol 116-31-4, **Retinal** 1406-18-4D, Vitamin E, derivs. 8044-71-1, Cetrimide 25322-68-3, Polyethylene-glycol 62996-74-1, Staurosporine 62996-74-1D, Staurosporine, derivs. 104987-12-4, Ascomycin 120685-11-2, PKC412 **212142-81-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Asakura, S; US 5385907 A 1995 HCAPLUS
(2) Liu, Y; US 2002173516 A1 2002 HCAPLUS
(3) Novartis Pharma Gmbh; WO 03074054 A 2003 HCAPLUS
(4) Univ Zhongshan Medical Ophthalmology; CN 1333018 A 2002 HCAPLUS
(5) Wakamoto Pharma Co Ltd; EP 1082966 A 2001 HCAPLUS
IT **212142-81-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ophthalmic** ointment composition comprising drug, ointment base and solubilizing dispersing agent)
RN 212142-81-9 HCAPLUS
CN 1-Phthalazinamine, N-(3-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:892619 HCAPLUS
DN 139:358815
ED Entered STN: 14 Nov 2003
TI Method using a phthalazine derivative for decreasing capillary permeability in the **retina** and for treating **diabetic** neuropathy
IN Brazzell, Romulus Kimbro; Green, Kenneth E.; Kane, Frances Elizabeth; **Campochiaro, Peter Anthony**
PA **Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-502
ICS A61P027-02
CC 1-12 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003092696	A1	20031113	WO 2003-EP4467	20030429 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRAI US 2002-376829P P 20020430 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003092696	ICM	A61K031-502
	ICS	A61P027-02

AB Methods are disclosed for decreasing or attenuating an increase in capillary permeability in the **retina** in a subject in need of such treatment, comprising administering a composition comprising an amount of a phthalazine derivative or salt thereof to a subject suffering from excessive

or pathol. capillary permeability in the **retina**, the amount of phthalazine derivative or salt being effective to decrease the permeability of capillaries in the **retina** of the subject, in particular where the subject is suffering from **macular edema.** The phthalazine derivs. include e.g. 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine. The phthalazine derivs. of the invention can also be used to treat **diabetic** neuropathy.

ST capillary permeability **retina macular edema** phthalazine deriv; pyridylmethyl phthalazine deriv capillary permeability **retina macular edema; diabetic** neuropathy phthalazine deriv

IT Blood
(-**retina** barrier; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT Nerve, disease
(**diabetic** neuropathy; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Vision**
(disorder, visual acuity loss; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye, disease**
(dominantly inherited cystoid **macular edema**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye, disease**
(**macular edema**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT Vein, disease
(occlusion, branch **retinal** vein occlusion, **macular edema** from; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT Drug delivery systems
(**ophthalmic**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT Biological transport
(permeation; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT Capillary vessel
Diabetes mellitus
Nervous system agents
(phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

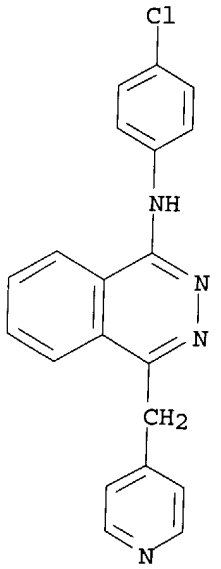
IT **Eye, disease**
(pseudophakic cystoid **macular edema**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye**
(**retina**, -**blood barrier**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye**
(**retina**; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye, disease**
(**retinopathy**, idiopathic **retinal** telangiectasia, **macular edema** from; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)

IT **Eye, disease**
(**uveitis**, intermediate, **macular edema**
from; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)
IT **Eye, disease**
(vitreomacular traction syndrome, **macular edema**
from; phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)
IT 253-52-1D, Phthalazine, derivs. **212141-54-3** 501901-70-8
501901-70-8D, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aiello, L; DIABETES 1997, V46(9) HCAPLUS
(2) Bold, G; DRUGS OF THE FUTURE 2002, V27(1), P43 HCAPLUS
(3) Fine, H; AMERICAN JOURNAL OF OPHTHALMOLOGY 2001, V132(5), P794 HCAPLUS
(4) Ici Ltd; EP 0002895 A 1979 HCAPLUS
(5) Kent, D; BRITISH JOURNAL OF OPHTHALMOLOGY 2000, V84(5), P542 MEDLINE
(6) Marj, W; WO 0009098 A 2000 HCAPLUS
(7) Mylari, B; US 2001056095 A1 2001
(8) Ozaki, H; EXPERIMENTAL EYE RESEARCH 1997, V64, P505 HCAPLUS
(9) Traxler, P; US 6258812 B1 2001 HCAPLUS
IT **212141-54-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phthalazine derivative for decreasing **retinal** capillary permeability and for treating **diabetic** neuropathy)
RN 212141-54-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:855697 HCAPLUS
DN 139:364941
ED Entered STN: 31 Oct 2003
TI Preparation of 3,4-diaminocyclobutene-1,2-diones as CXC chemokine receptor

antagonists

IN Taveras, Arthur G.; Aki, Cynthia J.; Bond, Richard W.; Chao, Jianping; Dwyer, Michael; Ferreira, Johan A.; Pachter, Jonathan A.; Baldwin, John J.; Kaiser, Bernd; Li, Ge; Merritt, J. Robert; Nelson, Kingsley H.; Rokosz, Laura L.

PA USA

SO U.S. Pat. Appl. Publ., 127 pp., Cont.-in-part of U.S. Ser. No. 62,006.
CODEN: USXXCO

DT Patent

LA English

IC ICM C07D277-56
ICS C07D263-34; C07D257-04; C07C225-18

NCL 544320000; 544408000; 546304000; 548194000; 548234000; 548254000; 548261000; 548309700; 548503000; 549434000

CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 25, 27, 63

FAN.CNT 2

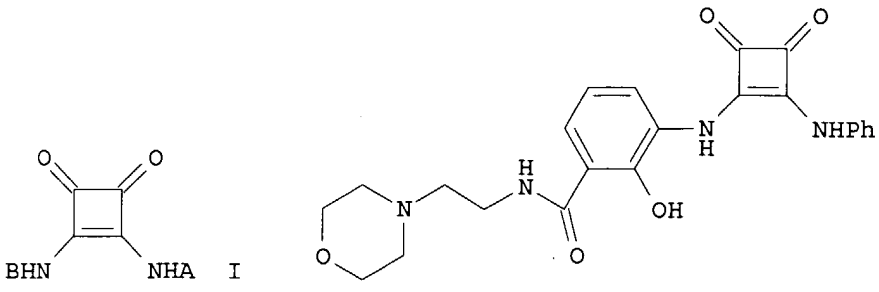
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003204085	A1	20031030	US 2002-208426	20020730 <--
US 2003097004	A1	20030522	US 2002-62006	20020201 <--
PRAI US 2001-265951P	P	20010202 <--		
US 2002-62006	A2	20020201 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003204085	ICM	C07D277-56
	ICS	C07D263-34; C07D257-04; C07C225-18
	NCL	544320000; 544408000; 546304000; 548194000; 548234000; 548254000; 548261000; 548309700; 548503000; 549434000
US 2003204085	ECLA	C07C225/20; C07D205/04; C07D207/08A; C07D207/16; C07D211/60; C07C229/42; C07C229/64; C07C; C07C237/44; C07C255/59; C07C271/20; C07C311/08; C07C311/21; C07D213/74D8; C07D213/89B; C07D235/06B; C07D239/42B1; C07D249/18; C07D277/28; C07D277/42; C07D285/08D; C07D295/12B1D4; C07D295/18B2F; C07D295/20B1; C07D317/66; C07D333/38 <--

OS MARPAT 139:364941

GI



AB Title compds. I [A = (substituted) aryl, heteroaryl; B = (substituted) Ph, benzotriazolyl, benzimidazolyl, hydroxyimidazolyl, hydroxythienyl, hydroxypyrrolyl, etc.], useful for treating chemokine mediated diseases selected from psoriasis, atopic dermatitis, asthma, arthritis, cancer, etc., were prepared Thus, 1-ethoxy-2-phenylamino-1-cyclobutene-3,4-dione (preparation given) and 2-OH-3-[(2-morpholinoethyl)aminocarbonyl]aniline (preparation given) were refluxed overnight in EtOH to give 34% title compound (II). I showed CXCR2 receptor binding activity in the range of 1-10000 nM. Pharmaceutical composition comprising the compound I is claimed.

ST aminobutenedione prepn CXC chemokine receptor antagonist; butenedione arylamino prepn CXC chemokine receptor antagonist; psoriasis atopic dermatitis asthma arthritis cancer treatment diaminobutenedione

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR1, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR2, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Intestine, disease
(Crohn's, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Sarcoma
(Kaposi's, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Respiratory distress syndrome
(acute, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Transplant rejection
(allotransplant, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Dermatitis
(atopic, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Stomach, neoplasm
(carcinoma, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Lung, disease
(chronic obstructive, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interleukin 12
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT **Eye, disease**
(**diabetic retinopathy**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Gingiva, disease
(gingivitis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Kidney, disease
(glomerulonephritis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Allergy
(hypersensitivity, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Hepatitis virus
Human herpesvirus
(infection treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Intestine, disease
(inflammatory, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Reperfusion
(injury, treatment of cardiac renal reperfusion injury; preparation of

3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Brain, disease
Heart, disease
(ischemia, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT **Eye, disease**
(**macula, degeneration**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Lung, neoplasm
(non-small-cell carcinoma, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT **Angiogenesis**
Angiogenesis inhibitors
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Anticoagulants
Antimalarials
Antitumor agents
Antiviral agents
Human
Immunosuppressants
Solid phase synthesis
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT **Eye, disease**
(**retinopathy**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Shock (circulatory collapse)
(septic, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Brain, disease
(stroke, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Shock (circulatory collapse)
(toxic shock syndrome, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Sepsis
(treatment of gram neg. sepsis; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT AIDS (disease)
Alzheimer's disease
Arthritis
Asthma
Atherosclerosis
Eye, disease
Malaria
Melanoma
Neoplasm
Psoriasis
Thrombosis
(treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Intestine, disease
(ulcerative colitis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Interleukin 8 receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 50-35-1, Thalidomide 145-63-1, Suramin 15866-90-7, Col-3 33069-62-4, Taxol 37270-94-3, Platelet factor 4 38101-59-6, Im862 86090-08-6, Angiostatin 99519-84-3, CAI 114977-28-5, Taxotere 129298-91-5, Tnp-470 148717-90-2, Squalamine 154039-60-8, Marimastat 169799-04-6, Cgs27023a 187888-07-9, Endostatin 188968-51-6, Emd121974 192329-42-3, Ag3340 204005-46-9, Su-5416 **212142-18-2**, **PTK 787** 216974-75-3 252916-29-3, Su-6668 259188-38-0, Bms-275291 305838-77-1, Neovastat 324740-00-3, Vitaxin 386211-13-8, Zd-101 443913-73-3, Zd-6474
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 52951-27-6P 378248-11-4P 378248-12-5P 464911-76-0P 464911-77-1P
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464912-83-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 62-53-3, Benzenamine, reactions 64-04-0, Benzeneethanamine 74-89-5, Methanamine, reactions 75-04-7, Ethanamine, reactions 85-38-1 87-62-7 88-75-5 90-41-5, [1,1'-Biphenyl]-2-amine 94-70-2 95-54-5, 1,2-Benzenediamine, reactions 95-55-6 96-50-4, 2-Thiazolamine 100-01-6, reactions 100-46-9, Benzenemethanamine, reactions 102-28-3 106-93-4 107-85-7 107-99-3 108-00-9 108-91-8, Cyclohexanamine, reactions 109-55-7 109-69-3 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 121-88-0 121-92-6 123-00-2, 4-Morpholinepropanamine 123-30-8 123-75-1, Pyrrolidine, reactions 124-40-3, reactions 124-68-5 142-25-6 303-38-8 372-19-0 372-39-4 462-08-8, 3-Pyridinamine 503-29-7, Azetidine 504-29-0, 2-Pyridinamine 536-90-3 540-54-5 552-89-6 570-23-0 582-33-2 587-02-0 591-27-5

606-22-4 615-36-1 619-14-7 626-43-7 643-28-7 645-36-3 873-74-5
931-16-8 1072-67-9, 3-Amino-5-methylisoxazole 2038-03-1,
4-Morpholineethanamine 2133-40-6 2217-41-6 2374-03-0 2491-20-5
2799-16-8 2799-17-9 2799-21-5 2835-98-5 2892-51-5 3218-02-8,
Cyclohexanemethanamine 3694-52-8 3958-60-9 4403-69-4 5231-87-8
5344-90-1 5680-79-5 14268-66-7, 1,3-Benzodioxol-5-amine 14338-36-4
14543-43-2 17467-15-1 17573-92-1, 3-Methoxythiophene 17720-99-9,
4-Thiazolamine 18638-99-8 23356-96-9 28059-64-5 32559-18-5
55586-26-0 57260-71-6 63435-16-5 68832-13-3 77648-20-5
95201-93-7, Methyl 3-hydroxy-4-bromo-2-thiophenecarboxylate 108267-20-5
112245-13-3 464913-93-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 608-32-2P, 1,2,3-Benzenetriamine 1202-00-2P 1214-44-4P 1668-84-4P,
1,3-Benzodioxol-4-amine 1904-62-7P 4331-29-7P, 1H-Benzimidazol-4-amine
4469-81-2P 5768-39-8P, 1,3-Benzodioxole-4-carboxylic acid 6299-39-4P
18076-61-4P, 1H-Benzotriazol-4-amine 18800-37-8P 20938-64-1P
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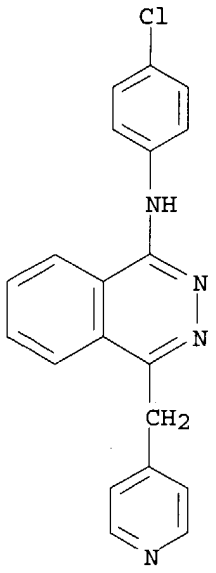
512190-85-1P 512190-87-3P 620098-31-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT **212142-18-2, PTK 787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 212141-54-3
CMF C20 H15 Cl N4



CM 2

CRN 110-15-6
CMF C4 H6 O4

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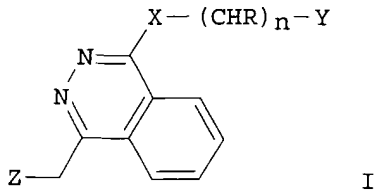
L80 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:717756 HCAPLUS
DN 139:246039
ED Entered STN: 12 Sep 2003
TI Preparation and use of phthalazines for treating **ocular neovascular** diseases
IN Brazzell, Romulus Kimbro
PA USA
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-503
NCL 514248000
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003171375	A1	20030911	US 2003-364606	20030211 <--
PRAI US 2002-356726P	P	20020213 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003171375	ICM	A61K031-503
	NCL	514248000

OS MARPAT 139:246039
GI



I

AB The invention relates to the use of certain phthalazines in the preparation of medicaments for the treatment of **ocular neovascularization.** The phthalazines, formula I (where n = 0-2, R = H or lower alkyl, X = imino, oxa, or thia, Y = aryl, and Z = pyridyl), are useful in treating diseases such as **choroidal neovascularization**, **retinal neovascularization**, exudative age related **macular degeneration**, proliferative **diabetic retinopathy**, and ischemic **retinopathy.** Thus, 1-(4-Chloroanilino)-4-(4-pridylmethyl)phthalazine hydrochloride was prepared by heating/refluxing a mixture of 0.972 g (3.8 mmol) 1-chloro-4-(4-pyridylmethyl)phthalazine, 0.656 g (4 mmol) 4-chloroaniline hydrochloride and 20 mL ethanol for 2 h; cooling in an ice bath; filtering; washing the crystallizate with a little ethanol and ether; and drying.

ST phthalazine compd prepn drug **eye ocular neovascular** disease

IT **Eye, disease**
(**diabetic retinopathy**; preparation of phthalazines for treating **ocular neovascular** diseases)

IT **Eye, disease**
(**macula, degeneration**; preparation of phthalazines for treating **ocular neovascular** diseases)

IT **Angiogenesis**
(**neovascularization**; preparation of phthalazines for treating **ocular neovascular** diseases)

IT Azines
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phthalazines; preparation of phthalazines for treating **ocular neovascular** diseases)

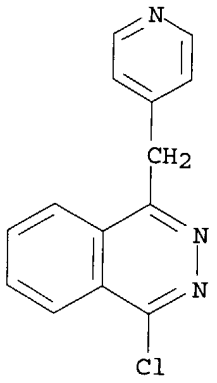
IT Human
(preparation of phthalazines for treating **ocular neovascular** diseases)

IT 106-47-8, 4-Chloroaniline, reactions 20265-96-7, 4-Chloroaniline hydrochloride **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation of phthalazines for treating **ocular neovascular** diseases)

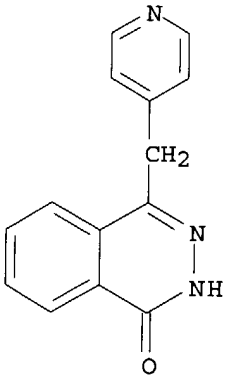
IT **212141-52-1P 212141-54-3P 212141-88-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazines for treating **ocular neovascular** diseases)

IT **212141-51-0 212141-57-6 212141-58-7**
212141-59-8 212141-60-1 212141-64-5
212141-66-7 212141-67-8 212141-68-9
212141-69-0 212141-70-3 212141-72-5
212141-73-6 212141-74-7 212141-75-8
212141-91-8 212141-92-9 212142-82-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of phthalazines for treating **ocular neovascular** diseases)

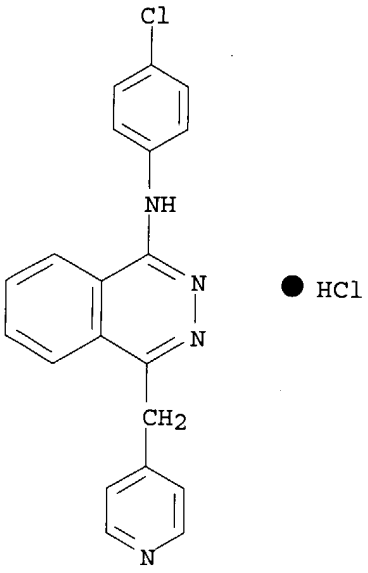
IT **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation of phthalazines for treating **ocular neovascular** diseases)
RN 101094-85-3 HCAPLUS
CN Phthalazine, 1-chloro-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



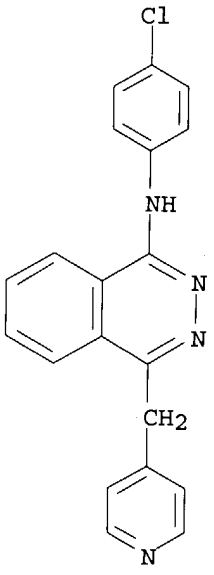
RN 107558-48-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



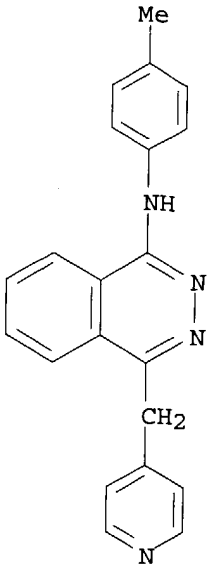
IT **212141-52-1P 212141-54-3P 212141-88-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazines for treating **ocular neovascular** diseases)
RN 212141-52-1 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



RN 212141-54-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

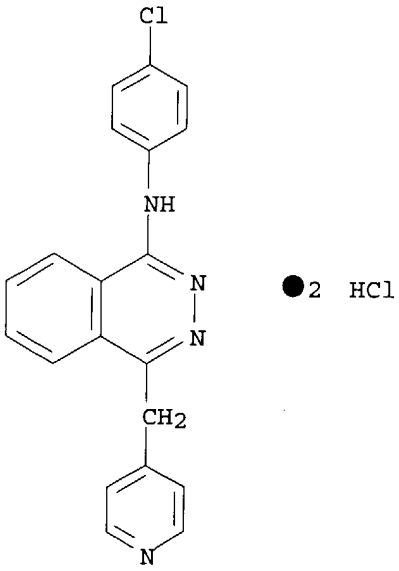


RN 212141-88-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-methylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

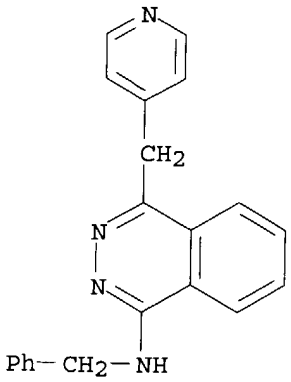


IT **212141-51-0 212141-57-6 212141-58-7**
212141-59-8 212141-60-1 212141-64-5
212141-66-7 212141-67-8 212141-68-9
212141-69-0 212141-70-3 212141-72-5
212141-73-6 212141-74-7 212141-75-8
212141-91-8 212141-92-9 212142-82-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of phthalazines for treating **ocular neovascular** diseases)

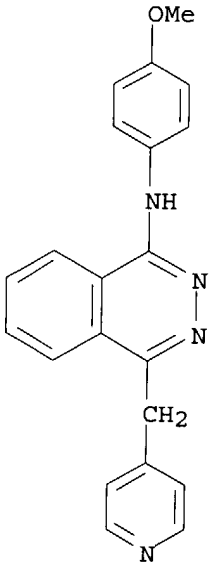
RN 212141-51-0 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



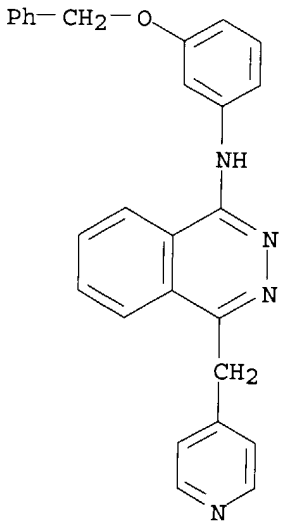
RN 212141-57-6 HCAPLUS
CN 1-Phthalazinamine, N-(phenylmethyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



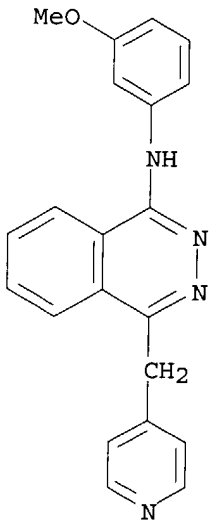
RN 212141-58-7 HCAPLUS
CN 1-Phthalazinamine, N-(4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



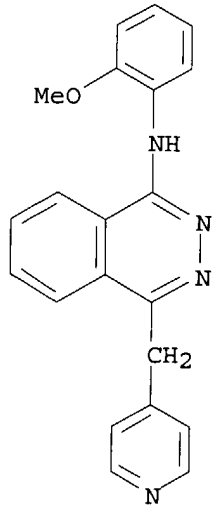
RN 212141-59-8 HCAPLUS
CN 1-Phthalazinamine, N-[3-(phenylmethoxy)phenyl]-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



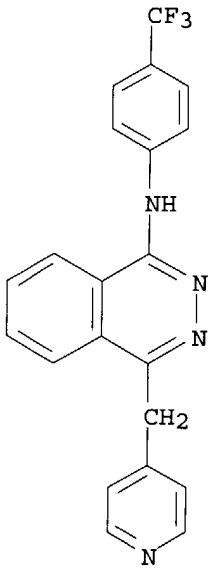
RN 212141-60-1 HCAPLUS
CN 1-Phthalazinamine, N-(3-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



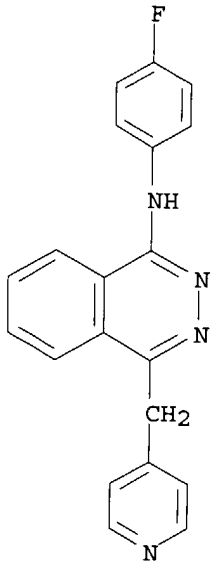
RN 212141-64-5 HCAPLUS
CN 1-Phthalazinamine, N-(2-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



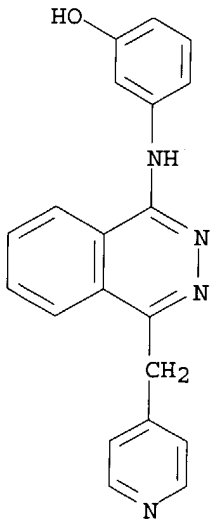
RN 212141-66-7 HCAPLUS
CN 1-Phthalazinamine, 4-(4-pyridinylmethyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



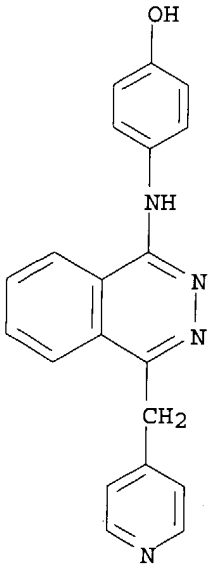
RN 212141-67-8 HCAPLUS
CN 1-Phthalazinamine, N-(4-fluorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



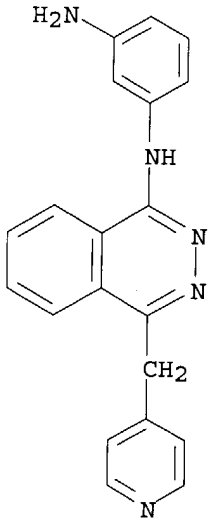
RN 212141-68-9 HCAPLUS
CN Phenol, 3-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



RN 212141-69-0 HCAPLUS
CN Phenol, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



RN 212141-70-3 HCAPLUS
CN 1,3-Benzenediamine, N-[4-(4-pyridinylmethyl)-1-phthalazinyl]- (9CI) (CA INDEX NAME)



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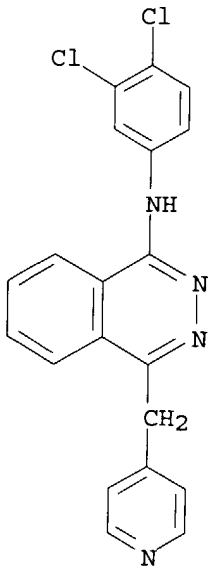
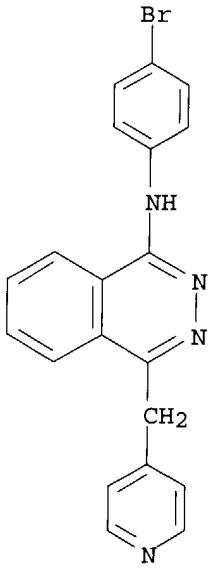
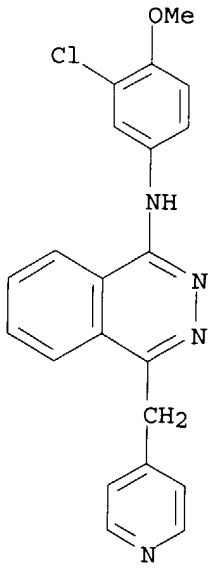
CN 1-Phthalazinamine, N-(3,4-dichlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



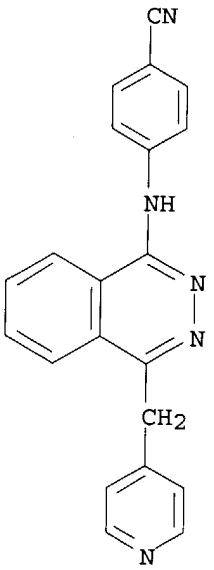
RN 212141-73-6 HCAPLUS
CN 1-Phthalazinamine, N-(4-bromophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



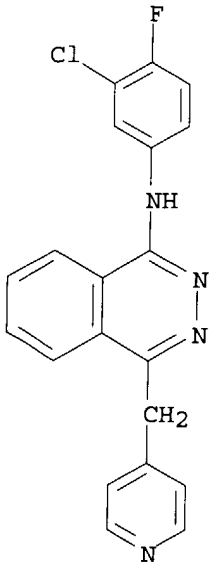
RN 212141-74-7 HCAPLUS
CN 1-Phthalazinamine, N-(3-chloro-4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



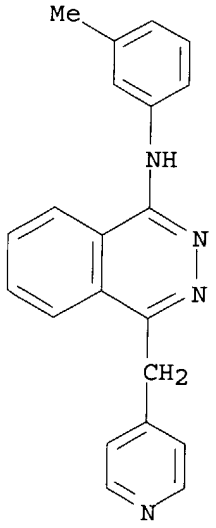
RN 212141-75-8 HCAPLUS
CN Benzonitrile, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



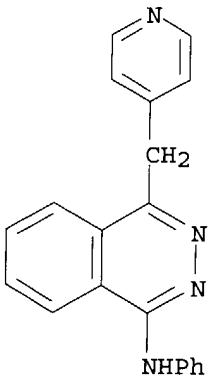
RN 212141-91-8 HCAPLUS
CN 1-Phthalazinamine, N-(3-chloro-4-fluorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-92-9 HCAPLUS
CN 1-Phthalazinamine, N-(3-methylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212142-82-0 HCAPLUS
CN 1-Phthalazinamine, N-phenyl-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:678790 HCAPLUS
DN 139:214477
ED Entered STN: 29 Aug 2003
TI Preparation of fused pyridazine derivatives as poly(ADP-ribose)polymerase inhibitors
IN Seko, Takuya; Takeuchi, Jun; Takahashi, Shinya; Kamanaka, Yoshihisa; Kamoshima, Wataru
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 368 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07D237-32
ICS C07D401-06; C07D401-12; C07D403-12; C07D405-06; C07D405-12; C07D409-12; C07D417-12; C07D471-04; C07D487-04; C07D513-04; A61K031-501; A61K031-502; A61K031-5025; A61K031-53; A61K031-5377; A61K031-541; A61K031-542; A61K031-55; A61K031-551
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003070707	A1	20030828	WO 2003-JP1694	20030218 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2002-42259 A 20020219 <--
JP 2002-199673 A 20020709 <--

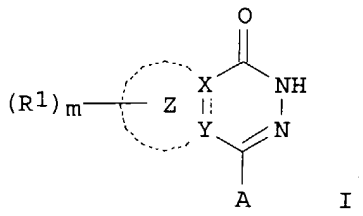
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003070707	ICM	C07D237-32
	ICS	C07D401-06; C07D401-12; C07D403-12; C07D405-06; C07D405-12; C07D409-12; C07D417-12; C07D471-04; C07D487-04; C07D513-04; A61K031-501; A61K031-502; A61K031-5025; A61K031-53; A61K031-5377; A61K031-541;

A61K031-542; A61K031-55; A61K031-551

OS MARPAT 139:214477

GI



I

AB The title compds. (I) and pharmaceutically acceptable salts thereof [R1 = H, C1-8 alkyl, C1-8 alkoxy, HO, halo, NO2, each optionally N-mono- or dialkylated NH2 or amino-C2-8 acyl, C2-8 acyl, phenyl-C1-8 alkoxy; X, Y = C, CH, N; a solid line accompanied by a dotted line is a single or double bond; the ring Z containing X and Y = each partially or completely saturated C3-10 monocyclic carbocyclic aryl or 3- to 10-membered monocyclic heterocyclic aryl containing 1-4 heteroatoms selected from O, N, and S; A = Q, Q1, Q2, Q3, etc.; wherein D1 = each N-(un)substituted NHCO, NHC(S), NHSO2, CH2NH, CH2NHCO, NHCONH, NH, NHCO2, NHC(S)NH, NH, or NHC(:NH), CH2O, OC(O); D2 = C1-8 alkylene, C2-8 alkenylene, Cyc2, -(C1-4 alkylene)-O-(C1-4 alkylene)-, -(C1-4 alkylene)-S-(C1-4 alkylene)-, -(C1-4 alkylene)-NH-(C1-4 alkylene)-, etc.; D3 = H, Cyc3, each (un)substituted NH2, CONH2, C(:CH)NH2, or NHC(:NH)NH2, OH, alkoxy, CO2H, alkoxycarbonyl, cyano, halo; G1 = C1-8 alkylene; G2 = H, C1-8 alkyl, C1-8 alkoxy, C2-8 acyl, Cyc6, NO2, Cyc6-C1-8 alkoxycarbonyl, -CO-Cyc6, etc.; R5 = H, C1-8 alkyl, C1-8 alkoxy, HO,NO2, each N-(un)substituted NH2 or amino-C1-8 alkyl, NHSO2OH, amidino, etc.; Cyc1, Cyc2, Cyc3, Cyc5, Cyc6 = groups each partially or completely saturated and monocyclic or bicyclic C3-10 carbocyclic aryl or 3- to 10-membered heterocyclic aryl containing 1-4 heteroatoms selected from O, N, and S] are prepared Because of inhibiting poly(ADP-ribose)polymerase, the compds. I are useful as preventives and/or remedies for various ischemic diseases (in brain, cord, heart, digestive tract, skeletal muscle, **retina**, etc.), inflammatory diseases (inflammatory bowel disease, multiple cerebrosclerosis, arthritis, etc.), neurodegenerative diseases (extrapyramidal disorder, Alzheimer's disease, muscular dystrophy, lumbar spinal canal stenosis, etc.), cataract, **diabetes**, **diabetes** complications, shock, head trauma, spinal cord injury, renal failure, and hyperalgesia. Moreover, these compds. are useful as agents against retroviruses (HIV, etc.) and sensitizers in treating cancer and immunosuppressants. Thus, a solution of 3-[bis(trimethylsilyl)amino]phenylmagnesium chloride in THF (1 M, 20.0 mL) was added to a solution of 3.04 g 3,4,5,6-tetrahydrophthalic anhydride in 40.0 mL THF at -78°, stirred for 1.5 h, treated with saturated aqueous NH4Cl solution, stirred at room temperature for 30 min to give, after workup, 3-(3-aminophenyl)-3-hydroxy-4,5,6,7-tetrahydro-2-benzofuran-1(3H)-one (II) as an oil. SOCl2 (5.20 mL) was added dropwise to 20.0 mL MeOH at -10°, stirred at 0° for 15 min, treated with II, stirred at room temperature for 18 h, concentrated, dissolved in 20 mL CH2Cl2, treated with Et3N, treated with H2O, and extracted with CH2Cl2 to give, after workup and silica gel chromatog., 3-(3-aminophenyl)-3-methoxy-4,5,6,7-tetrahydro-2-benzofuran-1(3H)-one (III). A solution of 2.56 g III and 503 mg hydrazine monohydrate in 30.0 mL EtOH was refluxed for 18 h, cooled to room temperature, and filtered to give, after washing the crystals obtained with hexane and drying, 32.0 mg 4-(3-aminophenyl)-5,6,7,8-tetrahydrophthalazine-1(2H)-one.

4-(3,5-Diaminophenyl)-6,7,9,9a-tetrahydro[1,4]thiazino[4,3-d][1,2,4]triazin-1(2H)-one, 8-(3-aminophenyl)-2,3,4,6-tetrahydropyrido[2,3-d]pyridazin-5(1H)-one mono- or dihydrochloride, and 4-[N-(2-aminoethyl)carbamoylmethyl]-5,6,7,8-tetrahydrophthalazin-1(2H)-one (IV) showed IC50 of 0.61, 0.10, and 0.29 μg/mL, resp. against poly(ADP-ribose)polymerase. A tablet and an ampule formulation containing IV were described.

ST fused pyridazine prepn poly ADP ribose polymerase inhibitor formulation; aminophenyltetrahydrophthalazinone prepn poly ADP ribose polymerase inhibitor; aminophenyltetrahydrothiazinotriazinone prepn poly ADP ribose polymerase inhibitor; aminophenyltetrahydropyridopyridazinone prepn poly ADP ribose polymerase inhibitor; aminoethylcarbamoylmethyltetrahydrophthalazinone prepn poly ADP ribose polymerase inhibitor; ischemia inflammation treatment prevention fused pyridazine prepn; neurodegenerative disease treatment prevention fused pyridazine prepn; cataract **diabetes** treatment prevention fused pyridazine prepn; shock cancer treatment prevention fused pyridazine prepn; retrovirus infection treatment prevention fused pyridazine prepn; phthalazinone prepn poly ADP ribose polymerase inhibitor; thiazinotriazinone prepn poly ADP ribose polymerase inhibitor; pyridopyridazinone prepn poly ADP ribose polymerase inhibitor

IT **Diabetes mellitus**
(complications; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Nervous system, disease
(degeneration; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Kidney, disease
(failure; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Pain
(hyperalgesia; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Brain, disease
(infarction; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Retroviridae
(infection; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Intestine, disease
(inflammatory; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Spinal cord, disease
(injury; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Brain, disease
Digestive tract, disease
Heart, disease
Muscle, disease
(ischemia; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Alzheimer's disease
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antitumor agents
Antiviral agents
Arthritis
Cataract
Diabetes mellitus
Human
Human immunodeficiency virus 1
Immunosuppressants
Inflammation
Ischemia
Muscular dystrophy
Neoplasm
Shock (circulatory collapse)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Antitumor agents
(sensitizers; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT Head, disease
(trauma; preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT 9055-67-8, Poly(ADP-ribose)polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

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590408-91-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT 590408-93-8P 590408-94-9P 590408-95-0P 590408-96-1P 590408-97-2P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT 62-53-3, Aniline, reactions 74-88-4, Methyl iodide, reactions 75-36-5, Acetyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-59-4, Phenylmagnesium chloride 107-30-2, Methoxymethyl chloride 110-85-0, Piperazine, reactions 121-90-4, 3-Nitrobenzoyl chloride 141-43-5, 2-Aminoethanol, reactions 400-94-2, 4-Fluoro-3-nitrobenzoyl chloride 407-25-0, Trifluoroacetic anhydride 591-51-5, Phenyllithium 699-98-9, Furo[3,4-b]pyridine-5,7-dione 998-40-3, Tri(n-butyl)phosphine 1003-03-8, Cyclopentylamine 1099-45-2, (Triphenylphosphoranylidene)aceti c acid ethyl ester 1118-03-2, Trimethyltin azide 1575-61-7, 5-Chloropentanoyl chloride 2426-02-0, 3,4,5,6-Tetrahydrophthalic anhydride 2605-67-6, (Triphenylphosphoranylidene)acetic acid methyl ester 4114-31-2, Hydrazinecarboxylic acid ethyl ester 4648-54-8, Trimethylsilyl azide 5717-37-3, 2-(Triphenylphosphoranylidene)propanoic acid ethyl ester 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride 7677-24-9, Trimethylsilyl cyanide 7803-57-8, Hydrazine monohydrate 10387-40-3, Potassium thioacetate 23590-60-5 51552-16-0 52770-24-8 57260-73-8 58729-31-0, Thiomorpholine-3-carboxylic acid ethyl ester 59648-15-6, Furo[3,4-d]pyridazine-5,7-dione 63024-77-1, 3-Chloromethylbenzoyl chloride 89775-56-4 89981-21-5 98303-20-9, 1-tert-Butoxycarbonylpiperidine-2-carboxylic acid 101166-65-8, 1-(tert-Butyldimethylsilyloxy)-2-iodoethane 124073-08-1 138371-65-0 174484-84-5, 3-[Bis(trimethylsilyl)amino]phenylmagnesium chloride 590409-14-6 590409-25-9 590409-31-7 590409-41-9 590409-42-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT 6538-81-4P 56475-18-4P 117436-83-6P 138371-52-5P 150348-51-9P
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590409-38-4P 590409-39-5P 590409-40-8P 590409-43-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

IT 590409-45-3P 590416-36-7P 590416-38-9P 590416-40-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Hahn, W; Acta Chim 1965, V10, P31 HCAPLUS
(2) Migliara, O; Journal of Heterocyclic Chemistry 1980, V17(3), P529 HCAPLUS
(3) Ono Pharmaceutical Co Ltd; WO 0044726 A 2000 HCAPLUS
(4) Ono Pharmaceutical Co Ltd; EP 1148053 A 2000 HCAPLUS

IT **590407-96-8P 590407-97-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused pyridazine derivs. as poly(ADP-ribose)polymerase inhibitors for treatment or prevention of diseases such as ischemia, inflammations and neurodegenerative diseases)

RN 590407-96-8 HCAPLUS
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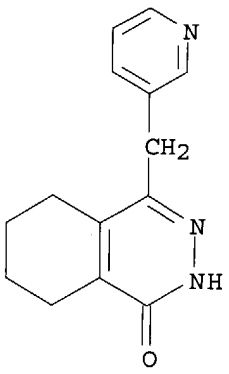

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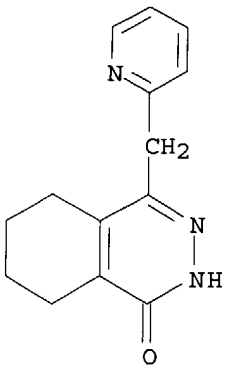

L80 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:551500 HCAPLUS
DN 139:117431
ED Entered STN: 18 Jul 2003
TI 4,5-Diamino-1,2,3,4-tetrahydro-3,6-pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer
IN Taveras, Arthur G.; Dwyer, Michael; Chao, Jianping; Baldwin, John J.; Merritt, Robert J.; Li, Ge; Chao, Jianhua; Yu, Younong
PA Schering Corporation, USA; Pharmacopeia, Inc.
SO PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D237-22
ICS C07D409-12; C07D405-12; C07D417-12; C07D403-12; A61K031-501; A61P035-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

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PI	WO 2003057676	A1	20030717	WO 2003-US299	20030103 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	EP 1461321	A1	20040929	EP 2003-705667	20030103 <--
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PRAI	US 2002-346248P	P	20020104 <--		
	US 2003-335789	A	20030102		
	WO 2003-US299	W	20030103		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003057676	ICM	C07D237-22
	ICS	C07D409-12; C07D405-12; C07D417-12; C07D403-12; A61K031-501; A61P035-00
US 2004063709	ECLA	C07D237/22; C07D403/12; C07D405/12; C07D405/12; C07D409/12; C07D417/12 <--

OS MARPAT 139:117431
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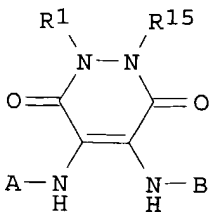

I

AB Prepns. for title compds. I [wherein R1 and R15 = independently H or (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl(alkyl), or

(hetero)arylalkyl; A = (un)substituted thiazolyl(alkyl), thienyl(alkyl), oxazolyl(alkyl), pyridinyl(alkyl), piperazinyl(alkyl), piperidinyl(alkyl), imidazolyl(alkyl), indolyl(alkyl), benzotriazolyl(alkyl), phenyl(alkyl), naphthyl(alkyl), carbamoylalkyl, etc.; B = (un)substituted Ph, benzotriazolyl, benzimidazolyl, indolyl, indazolyl, pyridinyl, pyrazolyl, thienyl, pyrrolyl, or pyrimidinyl; or pharmaceutically acceptable salts or solvates thereof] and their intermediates are disclosed (no data). In addition, CXCR1 SPA, CXCR2 SPA, calcium fluorescence, chemotaxis, and cytotoxicity assays are described. For example, 5-methylsalicylic acid was coupled with dimethylamine in the presence of DCC in EtOAc to give 2-hydroxy-N,N,5-trimethylbenzamide, which was nitrated (44%) and reduced using 10% Pd/C to give 3-amino-2-hydroxy-N,N,5-trimethylbenzamide (99%). The amine may be coupled with 1,2,3,4-tetrahydro-3,6-pyridazinediones to provide compds. of the invention (no data). I may exhibit a range of CXCR2 receptor binding activities from about 1 nM to about 10,100 nM. Thus, I and pharmaceutical compns. comprising I may be useful for the treatment of acute and chronic inflammatory disorders and cancer (no data).

ST pyridazinedione prepn CXC chemokine receptor antagonist antiinflammatory anticancer

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR1; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR2; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Intestine, disease
(Crohn's; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Sarcoma
(Kaposi's; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Respiratory distress syndrome
(acute; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Respiratory distress syndrome
(adult; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Transplant rejection
(allotransplant; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Eye, disease**
(**angiogenic**; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Cytotoxic agents
(antimetabolites, combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Dermatitis
(atopic; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Stomach, neoplasm
(carcinoma; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Lung, disease
(chronic obstructive; preparation of pyridazinediones as CXC chemokine

receptor antagonists for treatment of inflammatory disorders and cancer)

IT Alkylating agents, biological
Angiogenesis inhibitors
Radiotherapy
(combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Antibodies and Immunoglobulins
Hormones, animal, biological studies
Interleukin 12
Natural products, pharmaceutical
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Allergy
(delayed hypersensitivity; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Eye, disease**
(**diabetic retinopathy**; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Gingiva, disease
(gingivitis; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Kidney, disease
(glomerulonephritis; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Sepsis
(gram neg.; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Eye, disease**
(**inflammation**; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Intestine, disease
(inflammatory; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Reperfusion
(injury; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Brain, disease
(ischemia; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Eye, disease**
(**macula, degeneration**; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Angiogenesis**
(**neovascularization**, corneal; preparation of pyridazinediones as

CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT AIDS (disease)
Alzheimer's disease
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Anticoagulants
Antimalarials
Antitumor agents
Antiviral agents
Arthritis
Asthma
Atherosclerosis
Drug delivery systems
Hepatitis virus
Human
Human herpesvirus
Malaria
Melanoma
Neoplasm
Psoriasis
Thrombosis
(preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Heart
(reperfusion injury, ischemia; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Kidney
(reperfusion injury; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Virus
(respiratory; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT **Eye, disease**
(**retrolental fibroplasia**; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Shock (circulatory collapse)
(septic; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Lung, neoplasm
(small-cell carcinoma; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Brain, disease
(stroke; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Shock (circulatory collapse)
(toxic shock syndrome; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Intestine, disease
(ulcerative colitis; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, combination therapy; preparation of pyridazinediones as CXC

chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT 562102-64-1P 562102-65-2P 562102-66-3P 562102-67-4P 562102-68-5P
562102-69-6P 562102-70-9P 562102-71-0P 562102-72-1P 562102-74-3P
562102-76-5P 562102-78-7P 562102-80-1P 562102-82-3P 562102-84-5P
562102-86-7P 562102-88-9P 562102-90-3P 562102-91-4P 562102-93-6P
562102-95-8P 562102-97-0P 562102-99-2P 562103-01-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CXC chemokine receptor antagonist; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT 50-35-1, Thalidomide 145-63-1, Suramin 15866-90-7, Col-3 33069-62-4, Paclitaxel 37270-94-3, Platelet Factor-4 38101-59-6, IM862 86090-08-6, Angiostatin 99519-84-3, CAI 114977-28-5, Docetaxel 129298-91-5, TNP-470 148717-90-2, Squalamine 154039-60-8, Marimastat 169799-04-6, CGS27023A 179545-77-8, Bay 12-9566 187888-07-9, Endostatin 188968-51-6, EMD121974 192329-42-3, AG3340 204005-46-9, SU-5416 **212142-18-2**, **PTK-787** 252916-29-3, SU-6668 259188-38-0, BMS-275291 305838-77-1, Neovastat 324740-00-3, Vitaxin 386211-13-8, ZD-101 443913-73-3, ZD 6474
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT 3082-71-1P 5693-42-5P 6299-39-4P 6668-27-5P 18076-61-4P, 1H-Benzotriazol-4-amine 39639-98-0P 40023-86-7P 52063-83-9P
60166-83-8P 65686-95-5P 66952-81-6P 70978-09-5P 70978-44-8P
83948-35-0P 83948-38-3P 100245-03-2P 122902-99-2P 127292-42-6P
194413-46-2P 202825-94-3P 389628-28-8P 434307-26-3P 437768-45-1P
464912-84-3P 464912-85-4P 464912-88-7P 464913-11-9P 467231-62-5P
473730-93-7P 473730-95-9P 473731-31-6P 473731-53-2P 473731-54-3P
473731-55-4P 473731-56-5P 473731-57-6P 473731-62-3P 473731-63-4P
473731-64-5P 473731-65-6P 473731-87-2P 473732-07-9P 473732-08-0P
473732-09-1P 473732-42-2P 473732-43-3P 473732-45-5P 473732-57-9P
473732-81-9P 473732-82-0P 473732-83-1P 473732-84-2P 473732-85-3P
473732-90-0P 473732-92-2P 473732-94-4P 473732-95-5P 473733-20-9P
473733-88-9P 473733-89-0P 473733-90-3P 473733-91-4P 473733-92-5P
473734-05-3P 473734-07-5P 473734-24-6P 473735-56-7P 512188-02-2P
512188-05-5P 512188-06-6P 512188-07-7P 512188-08-8P 512188-09-9P
512188-10-2P 512188-11-3P 512188-12-4P 512188-13-5P 512188-15-7P
512188-17-9P 512188-18-0P 512188-19-1P 562103-03-1P 562103-08-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT 562103-09-7P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

IT 50-85-1, 4-Methylsalicylic acid 85-38-1, 3-Nitrosalicylic acid 89-56-5, 5-Methylsalicylic acid 98-03-3, 2-Thiophenecarboxaldehyde 98-98-6, Picolinic acid 100-52-7, Benzaldehyde, reactions 110-91-8, Morpholine, reactions 120-57-0, 3,4-Methylenedioxybenzaldehyde

123-11-5, 4-Methoxybenzaldehyde, reactions 123-75-1, Pyrrolidine, reactions 135-00-2, 2-Thienyl phenyl ketone 456-48-4, 3-Fluorobenzaldehyde 587-04-2, 3-Chlorobenzaldehyde 594-19-4, tert-Butyl lithium 620-02-0, 5-Methyl-2-furancarboxaldehyde 651-70-7, 2-(Trifluoroacetyl)thiophene 920-39-8, Isopropyl magnesium bromide 2026-48-4, (S)-2-Amino-3-methyl-1-butanol 2627-86-3 2689-59-0, 2-Furyl phenyl ketone 2799-21-5, (R)-(+)-3-Pyrrolidinol 3002-94-6, Cyclopropyl lithium 3082-64-2 3694-52-8, 3-Nitro-1,2-phenylenediamine 3886-69-9 4276-09-9, (D)-Valinol 4747-21-1, N-Methylisopropylamine 5271-67-0, 2-Thiophenecarbonyl chloride 7210-75-5, 2-Thiazolyl phenyl ketone 13745-17-0, 4-Bromopyrazole-3-carboxylic acid 20409-48-7, 2,2-Dimethyl-1-(thien-2-yl)-1-propanone 20980-22-7, 2-(Piperazin-1-yl)pyrimidine 22838-58-0 57260-71-6 62353-75-7 68832-13-3, (R)-(-)-2-Pyrrolidinemethanol 79852-25-8, 2-Thienyl cyclohexyl ketone 110013-19-9, (S)-3-Pyrrolidinemethanol 198348-89-9, 5-Nitro-3-pyrazolecarboxylic acid 473734-02-0, 4-Dimethylcarbamoylpiperazine-2-carboxylic acid ethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Nissan Chem Ind; EP 0275997 A 1988 HCAPLUS
(2) Nissan Chem Ind; EP 0376079 A 1990 HCAPLUS

IT **212142-18-2**, **PTK-787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of pyridazinediones as CXC chemokine receptor antagonists for treatment of inflammatory disorders and cancer)

RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

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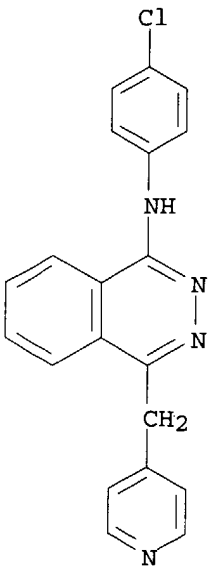
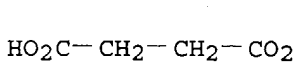
CRN 212141-54-3
CMF C20 H15 Cl N4



CM 2

CRN 110-15-6
CMF C4 H6 O4



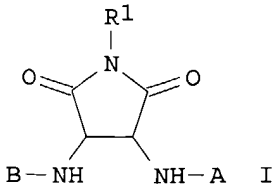
L80 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:301081 HCAPLUS
DN 138:321127
ED Entered STN: 18 Apr 2003
TI Preparation of 3,4-disubstituted maleimide compounds as CXC-chemokine receptor antagonists
IN Taveras, Arthur G.; Dwyer, Michael; Ferreira, Johan A.; Girijavallabhan, Viyyoor M.; Chao, Jianping; Baldwin, John J.; Merritt, J. Robert; Li, Ge
PA Schering Corporation, USA; Pharmacopeia, Inc.
SO PCT Int. Appl., 229 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D409-12
ICS C07D405-12; C07D207-44; C07D401-08; C07D403-12; C07D401-12; C07D409-14; C07D417-12; A61K031-4015; A61K031-4025; A61P035-00
CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003031440	A1	20030417	WO 2002-US32628	20021011 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004034229	A1	20040219	US 2002-269775	20021011 <--
EP 1434775	A1	20040707	EP 2002-786395	20021011 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI US 2001-329005P	P	20011012 <--		
WO 2002-US32628	W	20021011		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003031440	ICM	C07D409-12
	ICS	C07D405-12; C07D207-44; C07D401-08; C07D403-12; C07D401-12; C07D409-14; C07D417-12; A61K031-4015; A61K031-4025; A61P035-00

OS MARPAT 138:321127
GI



AB Disclosed are 3,4-disubstituted maleimides (shown as I; variables defined below; e.g. 3-[[3-(dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-((tert-butyl)amino)maleimide) or pharmaceutically acceptable salts or solvates thereof. The compds. are useful for the treatment of chemokine-mediated diseases such as acute and chronic inflammatory disorders and cancer. CXCR1 and CXCR2 SPA, calcium fluorescence, chemotaxis (for 293-CXCR2), cytotoxicity and soft agar receptor binding assay methods are described but no test results are reported. Although the methods of preparation are not claimed, 1 example preparation of I and a large number of example prepns. of intermediates are included; also >200 specific I are claimed. For I: R1 = H or (un)substituted aryl, heteroaryl, alkyl, arylalkyl, heteroarylalkyl, cycloalkyl, heterocycloalkyl, cycloalkylalkyl, and heterocycloalkylalkyl; A is selected from a very large group of possibilities, e.g. CR7R8Z (Z = (un)substituted pyridinyl, 1-oxopyridinyl, thiazolyl, furyl, oxazolyl, imidazolyl); B is selected from a very large group of possibilities, e.g. (un)substituted Ph, benzotriazol-7-yl, thienyl; addnl. details are given in the claims.

ST maleimide prepn CXC chemokine receptor antagonist

IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Anti-VEGF; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXC, antagonists; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR1, antagonists; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR2, antagonists; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Intestine, disease
(Crohn's; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Sarcoma
(Kaposi's, associated virus; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Pancreas, disease
(acute and chronic pancreatitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Respiratory distress syndrome
(acute; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Respiratory tract, disease
(adult; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Alkylation
(agents; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

IT Hepatitis
(alc., acute; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Liver, disease
(alc.; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Transplant rejection
(allotransplant; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT **Eye, disease**
(**angiogenic**; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-hormones; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)
IT Antiarteriosclerotics
(antiatherosclerotics; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Cytotoxic agents
(antimetabolites; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**
)
IT Dermatitis
(atopic; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Tongue, disease
(benign migratory glossitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Bronchi, disease
(bronchiectasis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Bronchi, disease
(bronchiolitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Stomach, neoplasm
(carcinoma; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Bronchi, disease
(chronic bronchitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Lung, disease
(chronic obstructive; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Hormones, animal, biological studies
Interleukin 12
Natural products, pharmaceutical
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)
IT Heart, disease
(cor pulmonale; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Artery, disease
(coronary, restenosis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Allergy
(delayed hypersensitivity; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT **Eye, disease**
(**diabetic retinopathy**; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Meninges
(disease, subarachnoid hemorrhage; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Intestine, disease
(duodenum, ulcer; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Breathing (animal)
(dyspnea; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Esophagus, disease
(esophagitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Lung, disease
(fibrosis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Gingiva, disease
(gingivitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Kidney, disease
(glomerulonephritis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Transplant and Transplantation
(graft-vs.-host reaction; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Sepsis
(gram neg.; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Respiratory tract, disease
(hyperresponsiveness; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Allergy
(hypersensitivity; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Hypoxia, animal
(hypoxemia; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT **Eye, disease**
(**inflammation**; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Intestine, disease
(inflammatory; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Reperfusion
(injury, transplant, cardiac and renal; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Lung, disease
(interstitial pneumonitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Brain, disease
Heart, disease
(ischemia; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT **Eye, disease**
(**macula, degeneration**; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT **Angiogenesis**
(**neovascularization**, corneal; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Lung, neoplasm
(non-small-cell carcinoma; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Respiratory tract, disease
(obstructive; preparation of 3,4-disubstituted maleimides as CXC-chemokine

receptor antagonists)
IT Periodontium, disease
(periodontitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Peritoneum, disease
(peritonitis, associated with continuous ambulatory peritoneal dialysis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Muscle, disease
(polymyositis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Parturition
(premature; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT AIDS (disease)
Acne
Allergy inhibitors
Alzheimer's disease
Angiogenesis
Angiogenesis inhibitors
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antimalarials
Antitumor agents
Antiulcer agents
Arthritis
Asthma
Atherosclerosis
Celiac disease
Common cold
Cough
Cystic fibrosis
Emphysema
Encephalitis
Gout
Hepatitis virus
Herpesviridae
Human
Human herpesvirus
Hypercapnia
Hypoxia, animal
Inflammation
Lupus erythematosus
Malaria
Melanoma
Meningitis
Multiple organ failure
Multiple sclerosis
Neoplasm
Osteoarthritis
Osteoporosis
Pruritus
Psoriasis
Sarcoidosis
(preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Intestine, disease
(pseudomembranous enterocolitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)
IT Arthritis

(psoriatic arthritis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Antihypertensives
Hypertension
(pulmonary; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Antiviral agents
Virus
(respiratory; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT **Eye, disease**
(**retinopathy**, of prematurity; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Heart, disease
(right ventricle, hypertrophy; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Shock (circulatory collapse)
(septic; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Respiratory tract, disease
(sinusitis, chronic; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Respiratory tract, disease
(small airway disease; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Injury
(strains, sprains and contusions; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Brain, disease
(stroke; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Lung
(surgical volume reduction; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Burn
(therapy; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Shock (circulatory collapse)
(toxic shock syndrome; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Brain, disease
Injury
(trauma; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Stomach, disease
(ulcer; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Intestine, disease
(ulcerative colitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Blood vessel, disease
(vasculitis, CNS; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Blood vessel, disease
(vasculitis; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Perfusion
(ventilation-perfusion mismatching; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Breathing (animal)
(wheezing; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Interleukin 8 receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, antagonists; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β, antagonists; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT 50-35-1, Thalidomide 145-63-1, Suramin 15866-90-7, Col-3 33069-62-4, Taxol 37270-94-3, Platelet Factor-4 38101-59-6, IM862 86090-08-6, Angiostatin 99519-84-3, CAI 114977-28-5, Taxotere 129298-91-5, TNP-470 148717-90-2, Squalamine 154039-60-8, Marimastat 169799-04-6, CGS27023A 179545-77-8, Bay 12-9566 187888-07-9, Endostatin 188968-51-6, EMD121974 192329-42-3, AG3340 204005-46-9, SU-5416 **212142-18-2**, **PTK-787** 252916-29-3, SU-6668 259188-38-0, BMS-275291 305838-77-1, Neovastat 324740-00-3, Vitaxin 386211-13-8, ZD-101 443913-73-3, ZD-6474
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

IT 512188-86-2P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-((tert-butyl)amino)maleimide 512188-87-3P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512188-88-4P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-((1-(furan-2-yl)ethyl)amino)maleimide 512188-89-5P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-(phenylamino)maleimide 512188-90-8P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-(cyclohexylamino)maleimide 512188-91-9P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-(cyclopentylamino)maleimide 512188-92-0P, 3-[[3-(Dimethylcarbamoyl)-2-hydroxyphenyl]amino]-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512188-93-1P, 3-[[3-((4-((Pyridin-2-yl)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-4-(((R)-1-phenylpropyl)amino)maleimide 512188-94-2P, 3-[[3-((2-Carboxy-4-((dimethylamino)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-4-(((R)-1-phenylpropyl)amino)maleimide 512188-95-3P, 3-[[3-((Dimethylamino)carbonyl)-2-hydroxyphenyl]amino]-4-(1-(benzodioxol-5-yl)propyl)maleimide 512188-96-4P, 3-[[3-(Aminocarbonyl)-2-hydroxyphenyl]amino]-4-(((R)-1-phenylpropyl)amino)maleimide 512188-97-5P, 3-[[3-((Morpholino)carbonyl)-2-hydroxyphenyl]amino]-4-(((R)-1-phenylpropyl)amino)maleimide 512188-98-6P, 3-[[3-((Dimethylamino)carbonyl)-2-hydroxyphenyl]amino]-4-((1-methylbutyl)amino)maleimide 512188-99-7P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino)-4-(((S)-1,2-dimethylpropyl)amino)maleimide 512189-00-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-ethyl-3-butynyl)amino)maleimide 512189-01-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-ethyl-2-propynyl)amino)maleimide 512189-02-5P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-03-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-04-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(3-fluorophenyl)propyl)amino)maleimide 512189-05-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)maleimide 512189-06-9P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)maleimide 512189-07-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)maleimide 512189-08-1P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-

phenylpropyl)amino)maleimide 512189-09-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)ethyl)amino)maleimide 512189-10-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)maleimide 512189-11-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)maleimide 512189-12-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-[((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino]maleimide 512189-13-8P, 3-((2-Hydroxy-3-((methylamino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-14-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((trans-2-methylcyclopentyl)amino)maleimide 512189-15-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((trans-2-phenylcyclohexyl)amino)maleimide 512189-16-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxy-6-methylphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-17-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512189-18-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512189-19-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cycloheptylamino)maleimide 512189-20-7P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512189-21-8P, 3-((6-((Dimethylamino)carbonyl)-5-hydroxypyrimidin-4-yl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-22-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512189-23-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)maleimide 512189-24-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((tert-butyl)amino)-1-methylmaleimide 512189-25-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-26-3P, 3-((1H-Benzotriazol-4-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-27-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((cyclopropyl)(thien-2-yl)methyl)amino)-1-methylmaleimide 512189-28-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(furan-2-yl)ethyl)amino)-1-methylmaleimide 512189-29-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(phenylamino)-1-methylmaleimide 512189-30-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclohexylamino)-1-methylmaleimide 512189-31-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclopentylamino)-1-methylmaleimide 512189-32-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2-dimethyl-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-33-2P, 3-((2-Hydroxy-3-((4-(pyrimidin-2-yl)piperazino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-34-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-ethylpropyl)amino)-1-methylmaleimide 512189-35-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-methylmaleimide 512189-36-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2-dimethyl-1-phenylpropyl)amino)-1-methylmaleimide 512189-37-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(4-methoxyphenyl)propyl)amino)-1-methylmaleimide 512189-38-7P, 3-((2-Hydroxy-3-((4-((pyridin-2-yl)carbonyl)piperazino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-39-8P, 3-((2-Hydroxy-3-((4-((thien-2-yl)carbonyl)piperazino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-40-1P, 3-((3-((2-Carboxy-4-((dimethylamino)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-41-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(benzodioxol-5-yl)propyl)amino)-1-methylmaleimide 512189-42-3P,

3-((3-(Aminocarbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-43-4P, 3-((2-Hydroxy-3-(((isopropyl)(methyl)amino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-44-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-45-6P, 3-((2-Hydroxy-3-((pyrrolidino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-46-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1,4-dimethylpentyl)amino)-1-methylmaleimide 512189-47-8P, 3-((2-Hydroxy-3-((morpholino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-48-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-methylbutyl)amino)-1-methylmaleimide 512189-49-0P, 3-((2-Hydroxy-3-(((S)-3-(hydroxymethyl)pyrrolidino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-50-3P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino)-4-(((S)-1,2-dimethylpropyl)amino)-1-methylmaleimide 512189-51-4P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-52-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-ethyl-3-butynyl)amino)-1-methylmaleimide 512189-53-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-ethyl-2-propynyl)amino)-1-methylmaleimide 512189-54-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-(cyclopropyl)(phenyl)methyl)amino)-1-methylmaleimide 512189-55-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(3-fluorophenyl)propyl)amino)-1-methylmaleimide 512189-56-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)-1-methylmaleimide 512189-57-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)-1-methylmaleimide 512189-58-1P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)-1-methylmaleimide 512189-59-2P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-60-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)ethyl)amino)-1-methylmaleimide 512189-61-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)-1-methylmaleimide 512189-62-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)-1-methylmaleimide 512189-63-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino)-1-methylmaleimide 512189-64-9P, 3-((1,6-Dihydro-4-hydroxy-6-oxopyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-65-0P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-66-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(thiazol-2-yl)propyl)amino)-1-methylmaleimide 512189-67-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-2-methoxy-1-phenylethyl)amino)-1-methylmaleimide 512189-68-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((phenylmethoxy)methyl)propyl)amino)-1-methylmaleimide 512189-70-7P, 3-((2-Hydroxy-3-((methylamino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-71-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((trans-2-(methoxymethyl)cyclohexyl)amino)-1-methylmaleimide 512189-72-9P 512189-73-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((trans-2-phenylcyclohexyl)amino)-1-methylmaleimide 512189-74-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxy-6-methylphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-75-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512189-76-3P, 3-((3-

((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512189-77-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(hydroxymethyl)-2-methylpropyl)amino)-1-methylmaleimide 512189-78-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(methoxymethyl)propyl)amino)-1-methylmaleimide 512189-79-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cycloheptylamino)-1-methylmaleimide 512189-80-9P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512189-81-0P, 3-((6-((Dimethylamino)carbonyl)-5-hydroxypyrimidin-4-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512189-82-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-methylmaleimide 512189-83-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)-1-methylmaleimide 512189-84-3P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-85-4P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512189-86-5P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)maleimide 512189-87-6P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)maleimide 512189-88-7P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)ethyl)amino)maleimide 512189-89-8P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)maleimide 512189-90-1P, 1-Ethyl-3-((5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-91-2P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)maleimide 512189-92-3P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino)maleimide 512189-93-4P, 1-Ethyl-3-((5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512189-94-5P, 1-Ethyl-3-((2-hydroxy-3-((methylamino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-95-6P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512189-96-7P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-methylbutyl)amino)maleimide 512189-97-8P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(furan-2-yl)ethyl)amino)maleimide 512189-98-9P, 1-Ethyl-3-((2-hydroxy-3-((morpholino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512189-99-0P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(phenylamino)maleimide 512190-00-0P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclohexylamino)maleimide 512190-01-1P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclopentylamino)maleimide 512190-02-2P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512190-03-3P, 1-Ethyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)maleimide 512190-04-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-phenylmaleimide 512190-05-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-phenylmaleimide 512190-06-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)-1-phenylmaleimide 512190-07-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)-1-phenylmaleimide 512190-08-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-

yl)ethyl)amino)-1-phenylmaleimide 512190-09-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)-1-phenylmaleimide 512190-10-2P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-phenylmaleimide 512190-11-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)-1-phenylmaleimide 512190-12-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino)-1-phenylmaleimide 512190-13-5P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-phenylmaleimide 512190-14-6P, 3-((2-Hydroxy-3-((methylamino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-phenylmaleimide 512190-15-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-phenylmaleimide 512190-16-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-methylbutyl)amino)-1-phenylmaleimide 512190-17-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(furan-2-yl)ethyl)amino)-1-phenylmaleimide 512190-18-0P, 3-((2-Hydroxy-3-((morpholino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-phenylmaleimide 512190-19-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(phenylamino)-1-phenylmaleimide 512190-20-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclohexylamino)-1-phenylmaleimide 512190-21-5P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclopentylamino)-1-phenylmaleimide 512190-22-6P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-phenylmaleimide 512190-23-7P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)-1-phenylmaleimide 512190-24-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-(phenylmethyl)maleimide 512190-25-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-(phenylmethyl)maleimide 512190-26-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)-1-(phenylmethyl)maleimide 512190-27-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)-1-(phenylmethyl)maleimide 512190-28-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)ethyl)amino)-1-(phenylmethyl)maleimide 512190-29-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)-1-(phenylmethyl)maleimide 512190-30-6P, 3-((5-Cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-(phenylmethyl)maleimide 512190-32-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)-1-(phenylmethyl)maleimide 512190-33-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino)-1-(phenylmethyl)maleimide 512190-34-0P, 3-((5-((Dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-(phenylmethyl)maleimide 512190-35-1P, 3-((2-Hydroxy-3-((methylamino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-(phenylmethyl)maleimide 512190-36-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-(phenylmethyl)maleimide 512190-37-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-methylbutyl)amino)-1-(phenylmethyl)maleimide 512190-38-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(furan-2-yl)ethyl)amino)-1-(phenylmethyl)maleimide 512190-39-5P, 3-((2-Hydroxy-3-((morpholino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-(phenylmethyl)maleimide 512190-40-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(phenylamino)-1-(phenylmethyl)maleimide 512190-41-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclohexylamino)-1-(phenylmethyl)maleimide 512190-42-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-

(cyclopentylamino)-1-(phenylmethyl)maleimide 512190-43-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)-1-(phenylmethyl)maleimide 512190-44-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)-1-(phenylmethyl)maleimide 512190-45-3P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-46-4P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512190-47-5P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)maleimide 512190-48-6P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((S)-1,2-dimethylpropyl)amino)maleimide 512190-49-7P
, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)ethyl)amino)maleimide 512190-50-0P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)maleimide 512190-51-1P, 1-Cyclohexyl-3-((5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-52-2P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-((isopropylamino)carbonyl)-2-methylpropyl)amino)maleimide 512190-53-3P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(((1-phenylethyl)amino)carbonyl)propyl)amino)maleimide 512190-54-4P, 1-Cyclohexyl-3-((5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512190-55-5P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)maleimide 512190-56-6P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-methylbutyl)amino)maleimide 512190-57-7P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-((1-(furan-2-yl)ethyl)amino)maleimide 512190-58-8P, 1-Cyclohexyl-3-((2-hydroxy-3-((morpholino)carbonyl)phenyl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-59-9P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(phenylamino)maleimide 512190-60-2P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclohexylamino)maleimide 512190-61-3P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(cyclopentylamino)maleimide 512190-62-4P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-2,2,2-trifluoro-1-(thien-2-yl)ethyl)amino)maleimide 512190-63-5P, 1-Cyclohexyl-3-((3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)propyl)amino)maleimide 512190-64-6P, 3-((3-((Dimethylamino)carbonyl)-1-methyl-4-((methylsulfonyl)amino)pyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-65-7P, 3-((3-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-66-8P, 3-((4-Amino-3-((dimethylamino)carbonyl)-1-methylpyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)maleimide 512190-67-9P, 3-((3-((Dimethylamino)carbonyl)-1-methyl-4-((methylsulfonyl)amino)pyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512190-68-0P, 3-((3-((Dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512190-69-1P, 3-((4-Amino-3-((dimethylamino)carbonyl)-1-methylpyrazol-5-yl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512190-70-4P, 3-((2-Hydroxyphenyl)amino)-4-(phenylamino)-1-methylmaleimide 512190-71-5P, 3-((2-Hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide 512190-72-6P, 3-((2-Hydroxyphenyl)amino)-4-(((R)-1-(thien-2-yl)propyl)amino)-1-methylmaleimide 512190-73-7P, 3-((2-Hydroxyphenyl)amino)-4-(((R)-1-(furan-2-yl)propyl)amino)-1-methylmaleimide 512190-74-8P, 3-((2-Hydroxyphenyl)amino)-4-(((S)-1,2,2-trimethylpropyl)amino)-1-methylmaleimide 512190-75-9P, 3-((2-Hydroxyphenyl)amino)-4-((trans-2-methylcyclopentyl)amino)-1-

methylmaleimide 512191-05-8P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)maleimide 512191-06-9P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-methylmaleimide 512191-07-0P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-benzylmaleimide 512191-08-1P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-phenylmaleimide 512191-09-2P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-benzylmaleimide 512191-10-5P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-methylmaleimide 512191-11-6P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)maleimide 512191-12-7P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-phenylmaleimide 512191-13-8P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)maleimide 512191-14-9P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-methylmaleimide 512191-15-0P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-benzylmaleimide 512191-16-1P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-phenylmaleimide 512191-17-2P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)maleimide 512191-18-3P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-methylmaleimide 512191-19-4P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-benzylmaleimide 512191-20-7P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-phenylmaleimide 512191-21-8P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)maleimide 512191-22-9P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-methylmaleimide 512191-23-0P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-phenylmaleimide 512191-24-1P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(benzodioxol-5-yl)-2,2-dimethylpropyl)amino)-1-benzylmaleimide 512191-25-2P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-benzylmaleimide 512191-26-3P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-phenylmaleimide 512191-27-4P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-benzylmaleimide 512191-28-5P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512191-29-6P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512191-30-9P, 3-((3-((Dimethylamino)sulfonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-phenylmaleimide 512191-31-0P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512191-32-1P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512191-33-2P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-benzylmaleimide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3,4-disubstituted maleimides as

CXC-chemokine receptor antagonists)

IT 512191-34-3P, 3-((3-(Dimethylphosphinyl)-2-hydroxyphenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-phenylmaleimide 512191-35-4P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512191-36-5P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512191-37-6P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-benzylmaleimide 512191-38-7P, 3-((2-Hydroxy-3-(N,N,N'-trimethylamidino)phenyl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-phenylmaleimide 512191-39-8P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)maleimide 512191-40-1P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-methylmaleimide 512191-41-2P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-phenylmaleimide 512191-42-3P, 3-((5-((Diethylamino)sulfonyl)-4-hydroxythien-3-yl)amino)-4-(((R)-1-(5-methylfuran-2-yl)propyl)amino)-1-benzylmaleimide 512191-43-4P, 3-((3-((Dimethylamino)carbonyl)-2-hydroxyphenyl)amino)-4-(((R)-1-phenylpropyl)amino)-1-methylmaleimide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT 386705-49-3, Vascular endothelial growth factor receptor kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

IT 50-85-1, 4-Methylsalicylic acid 62-53-3, Phenylamine, reactions 75-64-9, (tert-Butyl)amine, reactions 85-38-1, 3-Nitrosalicylic acid 89-56-5, 5-Methylsalicylic acid 98-03-3, Thiophene-2-carboxaldehyde 98-98-6, Picolinic acid 100-52-7, Benzaldehyde, reactions 103-49-1, Dibenzylamine 103-67-3, Benzyl(methyl)amine 106-48-9, 4-Chlorophenol 108-91-8, Cyclohexylamine, reactions 109-89-7, Diethylamine, reactions 110-91-8, Morpholine, reactions 120-57-0, 1,3-Benzodioxole-5-carboxaldehyde 120-83-2, 2,4-Dichlorophenol 123-11-5, 4-Methoxybenzaldehyde, reactions 123-75-1, Pyrrolidine, reactions 135-00-2, Phenyl(thien-2-yl)methanone 456-48-4, 3-Fluorobenzaldehyde 459-57-4, 4-Fluorobenzaldehyde 501-53-1, Benzyl chloroformate 587-04-2, 3-Chlorobenzaldehyde 594-19-4, tert-Butyllithium 609-70-1, 4-Hydroxynicotinic acid 616-24-0, (1-Ethylpropyl)amine 620-02-0, 5-Methylfuran-2-carboxaldehyde 651-70-7, 2-(Trifluoroacetyl)thiophene 920-39-8, Isopropylmagnesium bromide 927-77-5, Propylmagnesium bromide 1003-03-8, Cyclopentylamine 1011-11-6, trans-2-Phenylcyclohexylamine 1013-88-3, Benzophenone imine 1111-92-8, Dimethylphosphinic chloride 1122-17-4, 3,4-Dichloro-2,5-furandione 1123-61-1, 3,4-Dichloro-1-methylmaleimide 1193-54-0, 3,4-Dichloromaleimide 2627-86-3, (S)-1-Phenylethylamine 2689-59-0, (Furan-2-yl)(phenyl)methanone 2799-21-5, (R)-(+)-3-Pyrrolidinol 3002-94-6, Cyclopropyllithium 3082-64-2, (R)-1-Phenylpropylamine 3694-52-8, 3-Nitro-1,2-phenylenediamine 3876-05-9, 3,4-Dichloro-1-phenylmaleimide 3886-69-9, (R)-1-Phenylethylamine 4276-09-9, D-Valinol 4747-21-1, Isopropylmethylamine 5271-67-0, 2-Thiophenecarbonyl chloride 5452-35-7, Cycloheptylamine 5689-95-2, (1-Ethyl-2-propynyl)amine 6604-07-5, (trans-2-Methylcyclopentyl)amine 7210-75-5, Phenyl(thiazol-2-yl)methanone 14321-27-8 16114-24-2, 3,4-Dichloro-1-benzylmaleimide 17573-92-1, 3-Methoxythiophene 20409-48-7, 2,2-Dimethyl-1-(thien-2-yl)-1-propanone 20980-22-7, N-(Pyrimidin-2-yl)piperazine 22038-88-6, ((R)-1-(Thien-2-yl)ethyl)amine 22095-34-7, (1-(Furan-2-yl)ethyl)amine 22147-09-7, cis-2-Phenylcyclohexylamine 22526-46-1, ((S)-1,2-Dimethylpropyl)amine

22526-47-2, ((S)-1,2,2-Trimethylpropyl)amine 22838-58-0, N-Boc-D-valine 28250-45-5, trans-2-Hydroxymethylcyclohexylamine monohydrochloride 28292-43-5, (1,4-Dimethylpentyl)amine 30543-88-5, (1-Benzylpropyl)amine 40357-87-7, 4-Hydroxy-1-methyl-2(1H)-pyridinone 50343-26-5, 3,4-Dichloro-1-cyclohexylmaleimide 50392-78-4, (1-(Pyridin-4-yl)ethyl)amine 57260-71-6, N-Bocpiperazine 57883-06-4, ((R)-1-(Methoxymethyl)propyl)amine 59915-99-0, (1-(Furan-2-yl)propyl)amine 60289-68-1, (1-(Pyridin-4-yl)propyl)amine 62353-75-7, Methyl 3-methoxythiophene-2-carboxylate 63493-28-7, (1-Methylbutyl)amine 68005-54-9, (trans-2-(Methoxymethyl)cyclohexyl)amine 68832-13-3, (R)-(-)-2-Pyrrolidinemethanol 79852-25-8, Cyclohexyl(thien-2-yl)methanone 80875-24-7, ((R)-1-((Isopropylamino)carbonyl)-2-methylpropyl)amine 81097-48-5, N-Tosyl-6-azabicyclo[3.1.0]hexane 84547-84-2, 4-Bromopyrazole-1-methyl-5-carboxylic acid 91298-74-7, (S)-2-Methoxy-1-phenylethylamine 95201-93-7, Methyl 3-hydroxy-4-bromo-2-thiophenecarboxylate 101257-87-8, 4-Methylpyrimidin-5-ol 110013-19-9, (S)-3-Pyrrolidinemethanol 142559-11-3, ((R)-1-((Phenylmethoxy)methyl)propyl)amine 188772-70-5, ((R)-1-(Furan-2-yl)propyl)amine 198348-89-9, 5-Nitro-3-pyrazolecarboxylic acid 276702-25-1, N,N-Dimethyl-3-amino-6-chloro-2-hydroxybenzenesulfonamide 473732-80-8, ((Cyclopropyl)(thien-2-yl)methyl)amine 473733-15-2, ((R)-1-(Benzodioxol-5-yl)propyl)amine 473733-53-8, (1-(Thiazol-2-yl)propyl)amine 473734-02-0, 4-(Dimethylcarbamoyl)piperazine-2-carboxylic acid ethyl ester 512188-83-9, (1-Ethyl-3-butynyl)amine 512188-84-0, ((R)-1-(((1-Phenylethyl)amino)carbonyl)propyl)amine 512188-85-1, ((R)-2,2,2-Trifluoro-1-(thien-2-yl)ethyl)amine 512190-97-5, N,N-Dimethyl-3-amino-2-hydroxybenzenesulfonamide 512803-33-7, ((S)-1-((Thien-2-yl)methyl)propyl)amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

IT 3082-71-1P 5693-42-5P, ((Phenyl)(thien-2-yl)methyl)amine 6299-39-4P, 4-Nitro-1H-benzotriazole 6668-27-5P, (2-Methyl-1-phenylpropyl)amine 18076-61-4P, 1H-Benzotriazol-4-amine 20198-77-0P, 3,4-Dichloro-1-ethylmaleimide 39639-98-0P, N-(Pyridin-2-ylcarbonyl)piperazine 40023-86-7P, (1-(3-Chlorophenyl)propyl)amine 40297-12-9P, trans-2-Phenylcyclopentylamine monohydrochloride 52063-83-9P, N-(2-Thenoyl)piperazine 60166-83-8P, 3-Methoxythiophene-2-carboxylic acid 65686-95-5P, (2,2,2-Trifluoro-1-(thien-2-yl)ethyl)amine 66952-65-6P, N,N-Dimethyl-2-hydroxy-3-nitrobenzamide 66952-81-6P, N-(2-Hydroxy-3-aminobenzoyl)morpholine 70978-09-5P, N,N-Dimethyl-3-amino-2-hydroxy-5-methylbenzamide 70978-44-8P, N,N-Dimethyl-2-hydroxy-5-methyl-3-nitrobenzamide 83948-35-0P, (1-(4-Methoxyphenyl)propyl)amine 83948-38-3P, ((Furan-2-yl)(phenyl)methyl)amine 100245-03-2P, N,N-Dimethyl-2-hydroxy-5-methylbenzamide 110545-67-0P, Methyl 3-methoxy-4-bromo-2-thiophenecarboxylate 110545-68-1P, 3-Methoxy-4-bromo-2-thiophenecarboxylic acid 115151-94-5P, trans-2-Methylcyclopentylamine monohydrochloride 122902-99-2P, (R)-2-((tert-Butoxycarbonyl)amino)-N,3-dimethylbutanamide 127292-42-6P, (1-(Benzodioxol-5-yl)propyl)amine 184039-62-1P, 3-Methoxythiophene-2-sulfonyl chloride 194413-46-2P, N-Methyl-3-amino-2-hydroxybenzamide 202825-94-3P, (R)-2-Amino-N,3-dimethylbutanamide hydrochloride 389628-28-8P, N-tert-Butoxycarbonyl-N'-(pyridin-2-ylcarbonyl)piperazine 434307-26-3P 437768-45-1P, ((Phenyl)(thiazol-2-yl)methyl)amine 464912-84-3P, (R)-N-(2-Hydroxy-3-nitrobenzoyl)-2-pyrrolidinemethanol 464912-85-4P, (R)-N-(3-Amino-2-hydroxybenzoyl)-2-pyrrolidinemethanol 464912-88-7P, N-(2-Hydroxy-3-aminobenzoyl)pyrrolidine 464913-11-9P, N,N-Dimethyl-3-amino-2-hydroxybenzamide 464913-29-9P, N,N-Dimethyl-3-methoxy-4-bromo-2-thiophenecarboxamide 467231-62-5P, 3-Amino-2-hydroxybenzamide 473730-93-7P, N-Isopropyl-N-methyl-3-amino-2-hydroxybenzamide 473730-95-9P, N-(2-Hydroxy-3-aminobenzoyl)-(S)-3-pyrrolidinemethanol 473731-31-6P, (R)-N-(2-Hydroxy-3-aminobenzoyl)-3-pyrrolidinol 473731-53-2P, N,N-Dimethyl-2-hydroxy-5-iodo-3-

nitrobenzamide 473731-54-3P, N,N-Dimethyl-2-methoxy-5-iodo-3-nitrobenzamide 473731-55-4P, N,N-Dimethyl-5-cyano-2-methoxy-3-nitrobenzamide 473731-56-5P, N,N-Dimethyl-5-cyano-2-hydroxy-3-nitrobenzamide 473731-57-6P, N,N-Dimethyl-3-amino-5-cyano-2-hydroxybenzamide 473731-62-3P, N,N-Dimethyl-2-hydroxy-4-methylbenzamide 473731-63-4P, N,N-Dimethyl-2-hydroxy-5-iodo-4-methylbenzamide 473731-64-5P, N,N-Dimethyl-2-hydroxy-5-iodo-4-methyl-3-nitrobenzamide 473731-65-6P, N,N-Dimethyl-3-amino-2-hydroxy-4-methylbenzamide 473731-86-1P, N,N-Dimethyl-4-[(diphenylmethylene)amino]-3-methoxythiophene-2-carboxamide 473731-87-2P, N,N-Dimethyl-4-amino-3-hydroxythiophene-2-carboxamide 473732-07-9P, N,N-Dimethyl-4-bromo-1-methylpyrazole-5-carboxamide 473732-08-0P, N,N-Dimethyl-4-bromo-1-methyl-3-nitropyrazole-5-carboxamide 473732-09-1P, N,N-Dimethyl-4-hydroxy-1-methyl-3-nitropyrazole-5-carboxamide 473732-42-2P, (2R)-N-((S)-1-Phenylethyl)-2-amino-3-methylbutanamide monohydrochloride 473732-43-3P, (2R)-N-((R)-1-Phenylethyl)-2-amino-3-methylbutanamide monohydrochloride 473732-45-5P, (2R)-N-((R)-1-Phenylpropyl)-2-amino-3-methylbutanamide monohydrochloride 473732-57-9P, (1-(3-Fluorophenyl)propyl)amine 473732-81-9P, ((Cyclohexyl)(thien-2-yl)methyl)amine 473732-82-0P, (2,2-Dimethyl-1-(thien-2-yl)propyl)amine 473732-83-1P, ((3-Fluorophenyl)methylene)((1R)-2-methyl-1-(((trimethylsilyl)oxy)methyl)propyl)amine 473732-85-3P, (R)-1-(3-Fluorophenyl)propylamine 473732-87-5P, ((R)-(Cyclopropyl)(4-fluorophenyl)methyl)amine 473732-90-0P, (R)-1-(Thien-2-yl)propylamine 473732-92-2P, (R)-2,2-Dimethyl-1-(thien-2-yl)propylamine 473732-94-4P, (R)-1-(5-Methylfuran-2-yl)propylamine 473732-95-5P, (S)-1-(5-Methylfuran-2-yl)propylamine 473733-88-9P, N-tert-Butoxycarbonyl-N'-(2-thenoyl)piperazine 473733-89-0P, N-(2-Hydroxy-3-nitrobenzoyl)-N'-(2-thenoyl)piperazine 473733-90-3P, N-(3-Amino-2-hydroxybenzoyl)-N'-(2-thenoyl)piperazine 473733-91-4P, N-(2-Hydroxy-3-nitrobenzoyl)-N'-(pyridin-2-ylcarbonyl)piperazine 473733-92-5P, N-(3-Amino-2-hydroxybenzoyl)-N'-(pyridin-2-ylcarbonyl)piperazine 473734-05-3P, 4-(Dimethylcarbamoyl)-1-(2-hydroxy-3-nitrobenzoyl)piperazine-2-carboxylic acid ethyl ester 473734-06-4P, 1-(3-Amino-2-hydroxybenzoyl)-4-(dimethylcarbamoyl)piperazine-2-carboxylic acid ethyl ester 473734-07-5P, 1-(3-Amino-2-hydroxybenzoyl)-4-(dimethylcarbamoyl)piperazine-2-carboxylic acid 473734-24-6P, N-(3-Amino-2-hydroxybenzoyl)-N'-(pyrimidin-2-yl)piperazine 473734-34-8P, N-Tosyl-trans-2-phenylcyclopentylamine 473734-35-9P, trans-2-Ethylcyclopentylamine monohydrochloride 473734-36-0P, trans-2-Propylcyclopentylamine monohydrochloride 473734-37-1P, trans-2-Isopropylcyclopentylamine monohydrochloride 473735-04-5P, N,N-Dimethyl-6-amino-5-hydroxypyrimidine-4-carboxamide 473735-05-6P, N,N-Dimethyl-5-amino-4-hydroxypyridine-3-carboxamide 473735-06-7P, 5-Amino-4-hydroxy-1-methyl-2(1H)-pyridinone 473735-56-7P, 2,2,2-Trifluoro-1-(thien-2-yl)ethanone oxime 473736-96-8P, N,N,N'-Trimethyl-3-amino-2-hydroxybenzamidine 473736-98-0P, (3-Amino-2-hydroxyphenyl)dimethylphosphine oxide 512188-02-2P, (R)-N-(2-Hydroxy-3-nitrobenzoyl)-3-pyrrolidinol 512188-03-3P, N,N-Dimethyl-3-amino-4-hydroxy-1-methylpyrazole-5-carboxamide 512188-05-5P 512188-06-6P, N,N-Dimethyl-5-nitro-3-pyrazolecarboxamide 512188-07-7P, N,N-Dimethyl-1-methyl-5-nitro-3-pyrazolecarboxamide 512188-08-8P, N,N-Dimethyl-5-amino-1-methyl-3-pyrazolecarboxamide 512188-09-9P, N,N-Dimethyl-5-(benzyloxycarbonylamino)-1-methyl-3-pyrazolecarboxamide 512188-10-2P, N,N-Dimethyl-5-(benzyloxycarbonylamino)-1-methyl-4-nitro-3-pyrazolecarboxamide 512188-11-3P, N,N-Dimethyl-5-amino-1-methyl-4-[(methylsulfonyl)amino]-3-pyrazolecarboxamide 512188-12-4P, N,N-Dimethyl-4-amino-5-(benzyloxycarbonylamino)-1-methyl-3-pyrazolecarboxamide 512188-13-5P, N,N-Dimethyl-5-(benzyloxycarbonylamino)-1-methyl-4-[(methylsulfonyl)amino]-3-pyrazolecarboxamide 512188-14-6P, N,N-Dimethyl-5-amino-4-hydroxy-1-methyl-3-pyrazolecarboxamide 512188-15-7P, N,N-Dimethyl-5-(benzyloxycarbonylamino)-4-bromo-1-methyl-3-pyrazolecarboxamide 512188-16-8P, N,N-Dimethyl-5-(benzyloxycarbonylamino)-4-hydroxy-1-methyl-3-

pyrazolecarboxamide 512188-17-9P, N,N-Dimethyl-3-methoxythiophene-2-carboxamide 512188-18-0P, N,N-Dimethyl-3-methoxy-4-nitrothiophene-2-carboxamide 512188-19-1P, N,N-Dimethyl-3-hydroxy-4-nitrothiophene-2-carboxamide 512188-20-4P, 3-Chloro-1-cyclohexyl-4-[[3-(dimethylcarbamoyl)-2-hydroxyphenyl]amino]maleimide 512188-21-5P, 3-Chloro-4-[[3-((dimethylamino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-22-6P, 3-Chloro-4-[[3-(aminocarbonyl)-2-hydroxyphenyl]amino]maleimide 512188-23-7P, 3-Chloro-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-24-8P, 3-Chloro-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-26-0P, 3-Chloro-4-[[3-((4-((pyridin-2-yl)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-27-1P, 3-Chloro-4-[[3-((4-((dimethylamino)carbonyl)-2-carboxypiperazino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-28-2P, 3-Chloro-4-[(6-((dimethylamino)carbonyl)-5-hydroxypyrimidin-4-yl)amino]maleimide 512188-29-3P, 3-Chloro-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]maleimide 512188-30-6P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxythien-3-yl)amino]maleimide 512188-31-7P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino]maleimide 512188-32-8P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-2-hydroxy-6-methylphenyl)amino]maleimide 512188-33-9P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-1-methyl-4-((methylsulfonyl)amino)pyrazol-5-yl)amino]maleimide 512188-34-0P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-5-yl)amino]maleimide 512188-35-1P, 3-Chloro-4-[(4-amino-3-((dimethylamino)carbonyl)-1-methylpyrazol-5-yl)amino]maleimide 512188-36-2P, 3-Chloro-4-[[3-((dimethylamino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-37-3P, 3-Chloro-4-[[3-(aminocarbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-38-4P, 3-Chloro-4-[[3-(((isopropyl)(methyl)amino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-39-5P, 3-Chloro-4-[[3-((pyrrolidino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-40-8P, 3-Chloro-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-41-9P, 3-Chloro-4-[[3-(((S)-3-(hydroxymethyl)pyrrolidino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-42-0P, 3-Chloro-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-43-1P, 3-Chloro-4-[[3-((4-(pyrimidin-2-yl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-44-2P, 3-Chloro-4-[[3-((4-((pyridin-2-yl)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-45-3P, 3-Chloro-4-[[3-((4-((thien-2-yl)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-46-4P, 3-Chloro-4-[[3-((2-carboxy-4-((dimethylamino)carbonyl)piperazino)carbonyl)-2-hydroxyphenyl]amino]-1-methylmaleimide 512188-47-5P, 3-Chloro-4-[(6-((dimethylamino)carbonyl)-5-hydroxypyrimidin-4-yl)amino]-1-methylmaleimide 512188-48-6P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]-1-methylmaleimide 512188-49-7P, 3-Chloro-4-[(1,6-dihydro-4-hydroxy-1-methyl-6-oxopyridin-3-yl)amino]-1-methylmaleimide 512188-50-0P, 3-Chloro-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]-1-methylmaleimide 512188-51-1P, 3-Chloro-4-[(1H-benzotriazol-4-yl)amino]-1-methylmaleimide 512188-52-2P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxythien-3-yl)amino]-1-methylmaleimide 512188-53-3P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-3-yl)amino]-1-methylmaleimide 512188-54-4P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-2-hydroxy-6-methylphenyl)amino]-1-methylmaleimide 512188-55-5P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-1-methyl-4-((methylsulfonyl)amino)pyrazol-5-yl)amino]-1-methylmaleimide 512188-56-6P, 3-Chloro-4-[(3-((dimethylamino)carbonyl)-4-hydroxy-1-methylpyrazol-5-yl)amino]-1-methylmaleimide 512188-57-7P, 3-Chloro-4-[(4-amino-3-((dimethylamino)carbonyl)-1-methylpyrazol-5-yl)amino]-1-methylmaleimide 512188-58-8P, 3-Chloro-1-ethyl-4-[[3-

((dimethylamino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-59-9P, 3-Chloro-1-ethyl-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-60-2P, 3-Chloro-1-ethyl-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-61-3P, 3-Chloro-1-ethyl-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]maleimide 512188-62-4P, 3-Chloro-1-ethyl-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]maleimide 512188-63-5P, 3-Chloro-1-cyclohexyl-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-64-6P, 3-Chloro-1-cyclohexyl-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]maleimide 512188-65-7P, 3-Chloro-1-cyclohexyl-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]maleimide 512188-66-8P, 3-Chloro-1-cyclohexyl-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]maleimide 512188-68-0P, 3-Chloro-4-[[3-((dimethylamino)carbonyl)-2-hydroxyphenyl]amino]-1-phenylmaleimide 512188-69-1P, 3-Chloro-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]-1-phenylmaleimide 512188-70-4P, 3-Chloro-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]-1-phenylmaleimide 512188-71-5P, 3-Chloro-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]-1-phenylmaleimide 512188-72-6P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]-1-phenylmaleimide 512188-73-7P, 3-Chloro-4-[[3-((dimethylamino)carbonyl)-2-hydroxyphenyl]amino]-1-(phenylmethyl)maleimide 512188-74-8P, 3-Chloro-4-[[3-((morpholino)carbonyl)-2-hydroxyphenyl]amino]-1-(phenylmethyl)maleimide 512188-75-9P, 3-Chloro-4-[[3-((methylamino)carbonyl)-2-hydroxyphenyl]amino]-1-(phenylmethyl)maleimide 512188-76-0P, 3-Chloro-4-[(5-cyano-3-((dimethylamino)carbonyl)-2-hydroxyphenyl)amino]-1-(phenylmethyl)maleimide 512188-77-1P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]-1-(phenylmethyl)maleimide 512188-78-2P, 3-Chloro-4-[(2-hydroxyphenyl)amino]-1-methylmaleimide 512188-79-3P, 3-Chloro-4-[(5-((dimethylamino)carbonyl)-4-hydroxypyridin-3-yl)amino]maleimide 512188-81-7P, N-[(1R)-1-(3-Fluorophenyl)propyl]-(2R)-2-amino-3-methyl-1-butanol 512188-82-8P, trans-2-Methoxymethylcyclohexylamine monohydrochloride 512190-79-3P, N,N-Dimethyl-4-amino-3-hydroxythiophene-2-sulfonamide 512190-80-6P, N,N-Dimethyl-3-methoxythiophene-2-sulfonamide 512190-81-7P, N,N-Dimethyl-3-hydroxythiophene-2-sulfonamide 512190-83-9P, N,N-Dimethyl-4-bromo-3-hydroxythiophene-2-sulfonamide 512190-85-1P, N,N-Dimethyl-4-bromo-3-methoxythiophene-2-sulfonamide 512190-87-3P, N,N-Dimethyl-4-[(diphenylmethylene)amino]-3-methoxythiophene-2-sulfonamide 512190-89-5P, N,N-Dibenzyl-4-amino-3-hydroxythiophene-2-sulfonamide 512190-91-9P, N-Benzyl-N-methyl-4-amino-3-hydroxythiophene-2-sulfonamide 512190-93-1P, N-Benzyl-N-ethyl-4-amino-3-hydroxythiophene-2-sulfonamide 512190-95-3P, N,N-Diethyl-4-amino-3-hydroxythiophene-2-sulfonamide 512190-98-6P, N,N,N'-Trimethyl-2-hydroxy-3-nitrobenzamidine 512190-99-7P, N,N,N'-Trimethyl-2-methoxy-3-nitrobenzamidine 512191-00-3P, 2,4-Dichlorophenyl dimethylphosphinate 512191-01-4P, (5-Chloro-2-hydroxyphenyl)dimethylphosphine oxide 512191-02-5P, (5-Chloro-2-hydroxy-3-nitrophenyl)dimethylphosphine oxide 512191-03-6P, Dimethyl (5-chloro-2-hydroxyphenyl)phosphonate 512191-04-7P, ((R)-1-(Benzodioxol-5-yl)-2,2-dimethylpropyl)amine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 3,4-disubstituted maleimides as CXC-chemokine receptor antagonists)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Davis, P; JOURNAL OF MEDICINAL CHEMISTRY 1992, V35(1), P177 HCAPLUS
(3) Edward, F; WO 0021927 A 2000 HCAPLUS
(4) Hanaineh-Abdelnour, L; TETRAHEDRON 1999, V55(40), P11859 HCAPLUS
(5) Palovich, M; WO 0164208 A 2001 HCAPLUS

(6) Tillack, A; JOURNAL OF ORGANOMETALLIC CHEMISTRY 1994, V482(1-2), P85
HCAPLUS

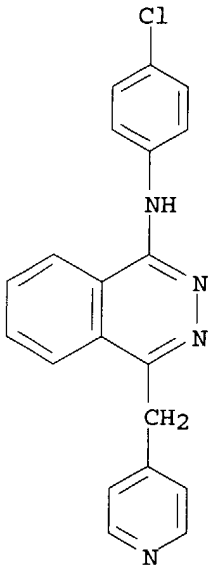
IT **212142-18-2, PTK-787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined with 3,4-disubstituted maleimide CXC-chemokine receptor antagonists useful against **angiogenesis**)

RN 212142-18-2 HCAPLUS

CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 212141-54-3
CMF C20 H15 Cl N4



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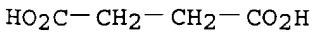

L80 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:868715 HCAPLUS

DN 137:346164

ED Entered STN: 15 Nov 2002

TI Anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents

IN Flowers, Clay; Saltman, David; Tam, Patrick M. S.; Burge, Clive T. R.; Harasym, Troy O.

PA Inex Pharmaceuticals Corporation, Can.

SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K009-127

CC 1-6 (Pharmacology)
Section cross-reference(s): 2, 15, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002089772	A1	20021114	WO 2002-US14608	20020509 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003082228	A1	20030501	US 2002-143545	20020509 <--
PRAI	US 2001-289935P	P	20010509 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002089772	ICM	A61K009-127

AB The present invention provides methods and compns. for the treatment and prevention of any of a large number of diseases and conditions with an **angiogenic** component, e.g., cancer. The present invention is based upon the discovery that liposome-encapsulated chemotherapeutic agents, such as alkaloids (e.g., vinca alkaloids such as vincristine), are surprisingly effective at treating such diseases or conditions when administered at a higher frequency than those used with conventional administration strategies. Such methods can be used to treat diseases such as cancer even when the cancer comprises cells that are resistant to the chemotherapeutic alkaloid. The liposome encapsulation of the chemotherapeutic agents, e.g., alkaloids, imparts dramatic improvements in the stability, biodistribution, and delivery of the agents, thereby allowing more efficacious and convenient administration to a patient with any of the herein-described diseases or conditions.

ST liposome encapsulated **antiangiogenic** therapy cancer chemotherapy

IT Calreticulin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino-terminal fragment (vasostatin); anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)

IT **Angiogenic** factors
Growth inhibitors, animal
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**angiogenic** growth-inhibiting factor; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)

IT **Angiogenesis**
Angiogenesis inhibitors
Anti-inflammatory agents
Antiglaucoma agents
Antirheumatic agents
Antitumor agents
Atherosclerosis
Human
Multiple myeloma
Neoplasm
Psoriasis
Rheumatoid arthritis
(anti-**angiogenic** therapy using liposome-encapsulated

chemotherapeutic agents for treatment of diseases such as cancer)
IT Alkaloids, biological studies
Growth factors, animal
Interleukin 12
Oligonucleotides
Thrombospondins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antiarteriosclerotics
(antiatherosclerotics; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Drug resistance
(antitumor; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Inflammation
(chronic; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Osteonectin
Osteopontin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cleavage product; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with ATTA and PEG; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Transplant and Transplantation
(cornea, failure; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Eye**
(**cornea**, **transplant**, failure; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Eye, disease**
(**diabetic retinopathy**; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antitumor agents
Blood vessel, neoplasm
(hemangioma; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Eye, disease**
(**keratitis**, interstitial; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid conjugates, liposomes containing; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Sphingomyelins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases

such as cancer)
IT Drug delivery systems
(liposomes; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Eye, disease**
(**macula, senile degeneration**; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antitumor agents
Neoplasm
(metastasis; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(meth 1; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antitumor agents
(multiple myeloma; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antitumor agents
(resistance to; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Artery, disease
(restenosis; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(restin; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Eye, disease**
(**retrolental fibroplasia**; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT **Glaucoma (disease)**
(rubeotic; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to vascular endothelial growth factor; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Blood vessel, disease
(vasculitis; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Blood vessel, disease
(vasculopathy; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Alkaloids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α; anti- **angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β; anti- **angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT 50-35-1, Thalidomide 57-22-7, Vincristine 865-21-4, Vinblastine 7689-03-4, Camptothecin 7689-03-4D, Camptothecin, analogs 9000-94-6D, Antithrombin III, fragment 9002-62-4D, Prolactin, derivative 15866-90-7, COL-3 37270-94-3D, Platelet factor 4, fragment 38101-59-6, IM862 71486-22-1, Vinorelbine 82855-09-2, Combretastatin 86090-08-6, Angiostatin 98724-27-7, Proliferin-related protein 99519-84-3, CAI 123948-87-8, Topotecan 129298-91-5, TNP-470 148717-90-2, Squalamine 154039-60-8, Marimastat 169799-04-6, CGS-27023A 187888-07-9, Endostatin 188968-51-6, EMD121974 192329-42-3, AG3340 194368-66-6, Angiopoietin 2 204005-46-9, SU5416 **212142-18-2**, **PTK787** 305838-77-1, Neovastat 324740-00-3, Vitaxin 474940-55-1, PIK 787/2K22584
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
IT 57-88-5, Cholesterol, biological studies 25322-68-3D, PEG, lipid conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Brahn; US 5583153 A 1996 HCAPLUS
(2) Choi; US 5820873 A 1998 HCAPLUS
(3) Ho; US 5714141 A 1998 HCAPLUS
(4) Von Borstel; US 5968914 A 1999 HCAPLUS
IT **212142-18-2**, **PTK787**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-**angiogenic** therapy using liposome-encapsulated chemotherapeutic agents for treatment of diseases such as cancer)
RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

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CRN 212141-54-3
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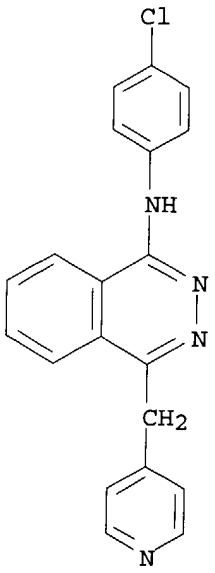

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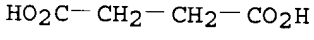

L80 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:754340 HCAPLUS
DN 137:279205
ED Entered STN: 04 Oct 2002
TI Preparation of 3,4-diaminocyclobutene-1,2-diones as CXC chemokine receptor antagonists
IN Taveras, Arthur G.; Aki, Cynthia J.; Bond, Richard W.; Chao, Jianping; Dwyer, Michael; Ferreira, Johan A.; Pachter, Jonathan; Baldwin, John J.; Kaiser, Bernd; Li, Ge; Merritt, J. Robert; Nelson, Kingsley H., Jr.; Rokosz, Laura L.
PA Schering Corporation, USA; Pharmacopeia, Inc.
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C225-20
ICS C07C229-42; C07C229-64; C07C237-36; C07C237-44; C07C255-58; C07C255-59; C07C271-20; C07C311-08; C07C311-21; C07D205-04; C07D207-08; C07D207-16; C07D211-60; C07D213-89; C07D231-38; C07D235-06; C07D239-42; C07D249-18; C07D277-28
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 25, 27
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002076926	A1	20021003	WO 2002-US2888	20020201 <--

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MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK,
SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
BR 2002006968 A 20040309 BR 2002-6968 20020201 <--
JP 2004529911 T2 20040930 JP 2002-576189 20020201 <--
NO 2003003424 A 20030930 NO 2003-3424 20030731 <--
PRAI US 2001-265951P P 20010202 <--
WO 2002-US2888 W 20020201 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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JP 2004529911	FTERM	4C023/HA03; 4C033/AD09; 4C033/AD13; 4C036/AD05; 4C036/AD16; 4C036/AD21; 4C036/AD27; 4C036/AD30; 4C054/AA02; 4C054/BB01; 4C054/CC04; 4C054/DD32; 4C054/EE01; 4C054/FF01; 4C055/AA01; 4C055/AA17; 4C055/BA01; 4C055/CA02; 4C055/CA52; 4C055/CB03; 4C055/CB15; 4C055/DA01; 4C063/AA01; 4C063/BB08; 4C063/BB09; 4C063/CC42; 4C063/CC81; 4C063/DD25; 4C063/DD42; 4C063/EE01; 4C069/AA02; 4C069/AA05; 4C069/BB02; 4C069/BB15; 4C069/BB22; 4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/BA13; 4C086/BB02; 4C086/BC02; 4C086/BC07; 4C086/BC17; 4C086/BC21; 4C086/BC36; 4C086/BC38; 4C086/BC42; 4C086/BC50; 4C086/BC60; 4C086/BC73; 4C086/BC82; 4C086/BC86; 4C086/GA02; 4C086/GA07; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA06; 4C086/ZA16; 4C086/ZA40; 4C086/ZA45; 4C086/ZA51; 4C086/ZA54; 4C086/ZA59; 4C086/ZA66; 4C086/ZA81; 4C086/ZA89; 4C086/ZA96; 4C086/ZB07; 4C086/ZB11; 4C086/ZB13; 4C086/ZB35; 4C086/ZB38; 4C086/ZC41; 4C206/AA01; 4C206/AA02; 4C206/AA03; 4C206/DA17; 4C206/DB15; 4C206/DB43; 4C206/FA31; 4C206/FA53; 4C206/GA02; 4C206/GA07; 4C206/GA22; 4C206/GA30; 4C206/GA31; 4C206/HA14; 4C206/HA22; 4C206/JA11; 4C206/MA01; 4C206/MA04; 4C206/NA14; 4C206/ZA06; 4C206/ZA16; 4C206/ZA40; 4C206/ZA45; 4C206/ZA51; 4C206/ZA54; 4C206/ZA59; 4C206/ZA66; 4C206/ZA81; 4C206/ZA89; 4C206/ZA96; 4C206/ZB07; 4C206/ZB11; 4C206/ZB13; 4C206/ZB35; 4C206/ZB38; 4C206/ZC41; 4H006/AA01; 4H006/AA03; 4H006/AB20; 4H006/AB22; 4H006/AB23; 4H006/AB24; 4H006/AB28; 4H006/BJ20; 4H006/BJ50; 4H006/BM30; 4H006/BM72; 4H006/BN30; 4H006/BR70; 4H006/BS10; 4H006/BT12; 4H006/BU26; 4H006/BU36; 4H006/BU46; 4H006/BV22; 4H006/BV25; 4H006/BV71; 4H006/BV72; 4H006/BV73; 4H006/BV74; 4H006/RA22; 4H006/RA38; 4H006/RA42

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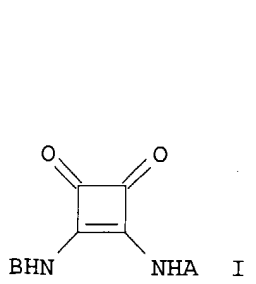

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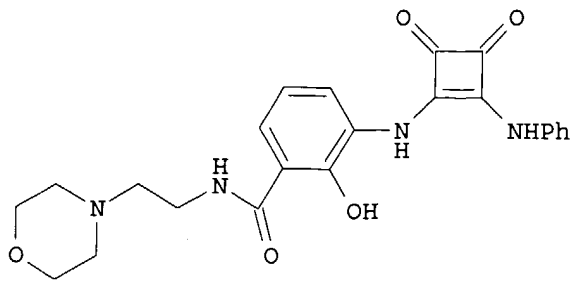

II

AB Title compds. I; [A = (substituted) aryl, heteroaryl; B = (substituted) Ph, benzotriazolyl, benzimidazolyl, hydroxyimidazolyl, hydroxythienyl, hydroxypyrrolyl, etc.], were prepared Thus, 1-ethoxy-2-phenylamino-1-cyclobutene-3,4-dione (preparation given) and 2-OH-3-[2-(morpholinoethyl)aminocarbonyl]aniline (preparation given) were refluxed overnight in EtOH to give 34% title compound (II). I showed CXCR2 receptor binding activity in the range of 1-10000 nM.

ST aminobutenedione prepn CXC chemokine receptor antagonist; butenedione arylamino prepn CXC chemokine receptor antagonist; psoriasis atopic dermatitis asthma arthritis cancer treatment diaminobutenedione

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR1, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CXCR2, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Intestine, disease
(Crohn's, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Sarcoma
(Kaposi's, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Respiratory distress syndrome
(acute, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Transplant rejection
(allotransplant, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Dermatitis
(atopic, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Stomach, neoplasm
(carcinoma, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Lung, disease
(chronic obstructive, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interleukin 12
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT **Eye, disease**
(**diabetic retinopathy**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Gingiva, disease
(gingivitis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Kidney, disease
(glomerulonephritis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Allergy
(hypersensitivity, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Hepatitis virus
Human herpesvirus
(infection treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Intestine, disease
(inflammatory, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Reperfusion
(injury, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Brain, disease
Heart, disease
(ischemia, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT **Eye, disease**
(**macula**, **degeneration**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Lung, neoplasm
(non-small-cell carcinoma, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Anti-AIDS agents
Anti-Alzheimer's agents
Antiarthritics
Antiasthmatics
Anticoagulants
Antimalarials
Antitumor agents
Antiviral agents
Human
Solid phase synthesis
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT **Eye, disease**
(**retinopathy**, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Shock (circulatory collapse)
(septic, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Brain, disease
(stroke, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Shock (circulatory collapse)
(toxic shock syndrome, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)
IT Sepsis
(treatment of gram neg. sepsis; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT AIDS (disease)
Alzheimer's disease
Arthritis
Asthma
Atherosclerosis
Eye, disease
Malaria
Melanoma
Neoplasm
Psoriasis
Thrombosis
(treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Intestine, disease
(ulcerative colitis, treatment; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT Interleukin 8 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β, antagonists; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 50-35-1, Thalidomide 145-63-1, Suramin 15866-90-7, Col-3 33069-62-4, Taxol 37270-94-3, Platelet factor 4 38101-59-6, Im862 86090-08-6, Angiostatin 99519-84-3, CAI 114977-28-5, Taxotere 129298-91-5, Tnp-470 148717-90-2, Squalamine 154039-60-8, Marimastat 169799-04-6, Cgs27023a 187888-07-9, Endostatin 188968-51-6, Emd121974 192329-42-3, Ag3340 204005-46-9, Su-5416 **212142-18-2**, **PTK 787** 216974-75-3 252916-29-3, Su-6668 259188-38-0, Bms-275291 305838-77-1, Neovastat 324740-00-3, Vitaxin 386211-13-8, Zd-101 443913-73-3, Zd-6474
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 52951-27-6P 378248-11-4P 378248-12-5P 464911-76-0P 464911-77-1P
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464912-83-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 62-53-3, Benzenamine, reactions 64-04-0, Benzeneethanamine 74-89-5, Methanamine, reactions 75-04-7, Ethanamine, reactions 75-29-6 85-38-1 87-62-7 88-75-5 89-57-6 90-04-0 90-41-5, [1,1'-Biphenyl]-2-amine 94-70-2 95-54-5, 1,2-Benzenediamine, reactions 95-55-6 96-50-4, 2-Thiazolamine 100-01-6, reactions 100-46-9, Benzenemethanamine, reactions 102-28-3 106-93-4 107-85-7 108-00-9 108-91-8, Cyclohexanamine, reactions 109-55-7 109-69-3 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 121-88-0 121-92-6 123-00-2, 4-Morpholinepropanamine 123-30-8 123-75-1, Pyrrolidine, reactions 124-40-3, reactions 124-68-5 142-25-6 303-38-8 372-19-0 372-39-4 462-08-8, 3-Pyridinamine 503-29-7, Azetidine 504-29-0, 2-Pyridinamine 536-90-3 552-89-6 570-23-0 578-54-1 582-33-2 587-02-0 591-27-5 606-22-4 615-36-1 619-14-7 626-43-7 643-28-7 645-36-3 873-74-5 931-16-8 1013-88-3 2038-03-1, 4-Morpholineethanamine 2133-40-6 2217-41-6 2237-30-1 2374-03-0 2491-20-5 2799-16-8 2799-17-9 2835-98-5 2892-51-5 2892-63-9 3218-02-8, Cyclohexanemethanamine 3694-52-8 3958-60-9 4403-69-4 4584-46-7 5222-73-1 5231-87-8 5344-90-1 5680-79-5 7195-78-0 14268-66-7, 1,3-Benzodioxol-5-amine 14338-36-4 14543-43-2 17467-15-1 17720-99-9, 4-Thiazolamine 18638-99-8 23356-96-9 28059-64-5 32559-18-5 55586-26-0 57260-71-6 63435-16-5 68832-13-3 77648-20-5 95201-93-7 108267-20-5 112245-13-3 146548-59-6 464913-93-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

IT 608-32-2P, 1,2,3-Benzenetriamine 1202-00-2P 1214-44-4P 1668-84-4P, 1,3-Benzodioxol-4-amine 1904-62-7P 4331-29-7P, 1H-Benzimidazol-4-amine 4469-81-2P 5768-39-8P, 1,3-Benzodioxole-4-carboxylic acid 6299-39-4P 18076-61-4P, 1H-Benzotriazol-4-amine 18800-37-8P 20938-64-1P 29026-74-2P 34801-09-7P 35748-34-6P 37073-18-0P 38177-30-9P 42132-07-0P 42132-09-2P 43200-31-3P 51736-38-0P 55581-64-1P 61292-50-0P 62723-78-8P 64039-56-1P 66952-81-6P 95539-61-0P 97962-70-4P 105337-21-1P 110545-67-0P 110545-68-1P 111081-10-8P 146224-62-6P 162046-50-6P 182500-29-4P 194413-46-2P 301527-63-9P 416876-80-7P 464912-84-3P 464912-85-4P 464912-87-6P 464912-88-7P 464912-89-8P 464912-90-1P 464912-91-2P 464912-92-3P 464912-93-4P 464912-94-5P 464912-96-7P 464912-98-9P 464913-01-7P 464913-03-9P 464913-05-1P 464913-08-4P 464913-11-9P 464913-13-1P 464913-15-3P 464913-17-5P 464913-19-7P 464913-21-1P 464913-23-3P 464913-25-5P 464913-29-9P 464913-33-5P 464913-35-7P 464913-37-9P 464913-40-4P 464913-42-6P 464913-44-8P 464913-48-2P 464913-50-6P 464913-53-9P 464913-55-1P 464913-57-3P 464913-59-5P 464913-60-8P 464913-61-9P 464913-63-1P 464913-65-3P 464913-67-5P 464913-69-7P 464913-71-1P 464913-73-3P 464913-74-4P 464913-75-5P 464913-76-6P 464913-77-7P 464913-78-8P 464913-79-9P 464913-80-2P 464913-81-3P 464913-82-4P 464913-83-5P 464913-84-6P 464913-85-7P 464913-86-8P 464913-87-9P 464913-88-0P 464913-89-1P 464913-90-4P 464913-91-5P 464913-92-6P 464913-94-8P 467231-62-5P 473731-86-1P 473731-87-2P 674790-13-7P 674791-42-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Beatrix, S; WO 0035864 A 2000 HCAPLUS
(2) Bi, G; WO 0192202 A 2001 HCAPLUS

(3) Chen, Y; HECHENG HUAXUE 1998, V6(4), P383 HCAPLUS
(4) Chen, Y; SICHUAN DAXUE XUEBAO, ZIRAN KEXUEBAN 1996, V33(2), P182 HCAPLUS
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(7) Huels Chemische Werke Ag; FR 1531943 A 1968 HCAPLUS
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(11) Neuse, E; POLYMER 1974, V15(1), P339
(12) Palovich, M; WO 0164208 A 2001 HCAPLUS

IT **212142-18-2, PTK 787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of 3,4-diaminobutene-1,2-diones as CXC chemokine receptor antagonists)

RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

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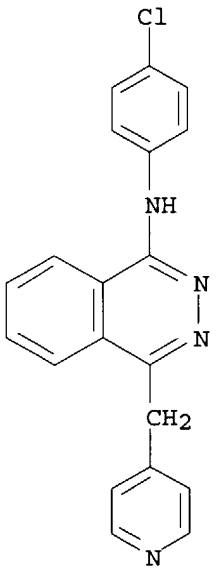
CRN 212141-54-3
CMF C20 H15 Cl N4



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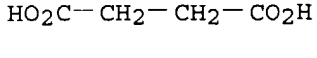
CRN 110-15-6
CMF C4 H6 O4



L80 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:935442 HCAPLUS
DN 136:74621
ED Entered STN: 28 Dec 2001
TI Combinations and compositions which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use

IN Siemeister, Gerhard; Haberey, Martin; Thierauch, Karl-Heinz
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K045-06
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2001097850	A2	20011227	WO 2001-EP6976	20010620	<--
	WO 2001097850	A3	20021212			
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	EP 1166799	A1	20020102	EP 2000-250214	20000628	<--
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	EP 1292335	A2	20030319	EP 2001-965012	20010620	<--
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	BR 2001011861	A	20031223	BR 2001-11861	20010620	<--
	EE 200200706	A	20040615	EE 2002-706	20010620	<--
	US 2003055006	A1	20030320	US 2001-887527	20010625	<--
	BG 107396	A	20030731	BG 2002-107396	20021217	<--
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	US 2004147449	A1	20040729	US 2004-796174	20040310	<--
PRAI	EP 2000-250194	A	20000623	<--		
	EP 2000-250214	A	20000628	<--		
	WO 2001-EP6976	W	20010620	<--		
	US 2001-887527	B1	20010625	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 2001097850	ICM	A61K045-06	
US 2003055006	ECLA	A61K045/06	<--

OS MARPAT 136:74621
AB The present invention describes the combination of substances interfering with the biol. activity of Vascular Endothelial Growth Factor (VEGF)/VEGF receptor systems (compound I) and substances interfering with the biol. function of Angiopoietin/Tie receptor systems (compound II) for inhibition of vascularization and for cancer treatment.
ST **angiogenesis** inhibitor antitumor VEGF receptor angiopoietin
IT Tyrosine kinase receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Tie; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)
IT Edema
(VEGF-associated; compns. which interfere with VEGF/VEGF receptor a

angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Blood vessel, neoplasm
(angiofibroma; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Antiarteriosclerotics
(antiatherosclerotics; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT **Angiogenesis** inhibitors
Antiarthritics
Antirheumatic agents
Antitumor agents
Apoptosis
Arteriosclerosis
Arthritis
Cirrhosis
Drug delivery systems
Drug delivery systems
Eye, disease
Fibrosis
Kidney, disease
Melanoma
Necrosis
Protein sequences
Psoriasis
Rheumatoid arthritis
Signal transduction, biological
Transplant rejection
cDNA sequences
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Vascular endothelial growth factor receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Antibodies and Immunoglobulins
Antibodies and Immunoglobulins
Oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Kidney, disease
(**diabetic** nephropathy; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT **Eye, disease**
(**diabetic retinopathy**; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Blood vessel
(endothelium, targeting of; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Kidney, disease
(glomerulonephritis; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Kidney, disease
(glomerulus; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as

angiogenesis inhibitors)

IT Blood vessel, neoplasm
(hemangioma; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Ascites
(inhibitors; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Nerve, disease
(injury; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand binding by; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Drug delivery systems
(liposomes; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT **Glaucoma (disease)**
(**neovascular**; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Kidney, disease
(nephrosclerosis, malignant; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptides; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Disease, animal
(proliferative; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT Ligands
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor binding by; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT 383438-60-6
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT 127464-60-2, Vascular endothelial growth factor 250740-90-0, Angiopoietin
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT **212142-18-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT 340830-03-7, Receptor tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT 383438-01-5, DNA (human clone WO-01/97850A2-SEQID2) 383438-02-6, DNA (human clone WO-01/97850A2-SEQID3) 383438-03-7, DNA (human clone WO-01/97850A2-SEQID1) 383438-04-8, DNA (human clone WO-01/97850A2-SEQID4) 383438-05-9, DNA (human clone WO-01/97850A2-SEQID5) 383438-06-0, DNA (human clone WO-01/97850A2-SEQID6) 383438-07-1, DNA (human clone WO-01/97850A2-SEQID7) 383438-08-2, DNA (human clone WO-01/97850A2-SEQID8) 383438-09-3, DNA (human clone WO-01/97850A2-SEQID9) 383438-10-6, DNA (human clone WO-01/97850A2-SEQID10) 383438-11-7, DNA (human clone WO-01/97850A2-SEQID11) 383438-12-8, DNA (human clone WO-01/97850A2-SEQID12) 383438-13-9, DNA (human clone WO-01/97850A2-SEQID13) 383438-14-0, DNA (human clone WO-01/97850A2-SEQID14) 383438-15-1, DNA (human clone WO-01/97850A2-SEQID15) 383438-16-2, DNA (human clone WO-01/97850A2-SEQID16) 383438-17-3, DNA (human clone WO-01/97850A2-SEQID17) 383438-18-4, DNA (human clone WO-01/97850A2-SEQID18) 383438-19-5, DNA (human clone WO-01/97850A2-SEQID19) 383438-20-8, DNA (human clone WO-01/97850A2-SEQID20) 383438-21-9, DNA (human clone WO-01/97850A2-SEQID21) 383438-22-0, DNA (human clone WO-01/97850A2-SEQID22) 383438-23-1, DNA (human clone WO-01/97850A2-SEQID23) 383438-24-2, DNA (human clone WO-01/97850A2-SEQID24) 383438-25-3, DNA (human clone WO-01/97850A2-SEQID25) 383438-26-4, DNA (human clone WO-01/97850A2-SEQID26) 383438-27-5, DNA (human clone WO-01/97850A2-SEQID27) 383438-28-6, DNA (human clone WO-01/97850A2-SEQID28) 383438-29-7, DNA (human clone WO-01/97850A2-SEQID29) 383438-30-0, DNA (human clone WO-01/97850A2-SEQID30) 383438-31-1, DNA (human clone WO-01/97850A2-SEQID31) 383438-32-2, DNA (human clone WO-01/97850A2-SEQID32) 383438-33-3, DNA (human clone WO-01/97850A2-SEQID33) 383438-34-4, DNA (human clone WO-01/97850A2-SEQID34) 383438-35-5, DNA (human clone WO-01/97850A2-SEQID35) 383438-36-6, DNA (human clone WO-01/97850A2-SEQID36) 383438-37-7, DNA (human clone WO-01/97850A2-SEQID37) 383438-38-8, DNA (human clone WO-01/97850A2-SEQID38) 383438-39-9, DNA (human clone WO-01/97850A2-SEQID39) 383438-40-2, DNA (human clone WO-01/97850A2-SEQID40) 383438-41-3, DNA (human clone WO-01/97850A2-SEQID41) 383438-42-4, DNA (human clone WO-01/97850A2-SEQID42) 383438-43-5, DNA (human clone WO-01/97850A2-SEQID43) 383438-44-6, DNA (human clone WO-01/97850A2-SEQID44) 383438-45-7, DNA (human clone WO-01/97850A2-SEQID45) 383438-46-8, DNA (human clone WO-01/97850A2-SEQID46) 383438-47-9, DNA (human clone WO-01/97850A2-SEQID47) 383438-48-0, DNA (human clone WO-01/97850A2-SEQID48) 383438-49-1, DNA (human clone WO-01/97850A2-SEQID49) 383438-50-4, DNA (human clone WO-01/97850A2-SEQID50) 383438-51-5, DNA (human clone WO-01/97850A2-SEQID51) 383438-52-6, DNA (human clone WO-01/97850A2-SEQID52) 383438-53-7, DNA (human clone WO-01/97850A2-SEQID53) 383438-54-8, DNA (human clone WO-01/97850A2-SEQID54) 383438-55-9, DNA (human clone WO-01/97850A2-SEQID54) 383438-56-0, DNA (human clone WO-01/97850A2-SEQID56) 383438-57-1, DNA (human clone WO-01/97850A2-SEQID57) 383438-58-2, DNA (human clone WO-01/97850A2-SEQID58) 383438-59-3, DNA (human clone WO-01/97850A2-SEQID59)

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleotide sequence; compns. which interfere with VEGF/VEGF receptor

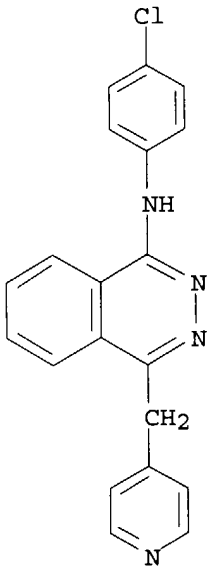
and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

IT **212142-18-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. which interfere with VEGF/VEGF receptor and angiopoietin/Tie receptor function and their use as **angiogenesis** inhibitors)

RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 212141-54-3
CMF C20 H15 Cl N4



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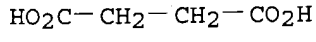
CMF C4 H6 O4



L80 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:747637 HCAPLUS
DN 135:269444
ED Entered STN: 12 Oct 2001
TI Improved treatment of **neovascularization**
IN Brazzell, Romulus Kimbro
PA **Novartis Ag, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.**
SO PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K041-00

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63

FAN.CNT 1

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PI	WO 2001074389	A2	20011011	WO 2001-EP3265	20010322 <--
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	ZA 2002007638	A	20031016	ZA 2002-7638	20020923 <--
PRAI	US 2000-191807P	P	20000324 <--		
	WO 2001-EP3265	W	20010322 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001074389	ICM	A61K041-00

AB The present invention describes an improved photodynamic treatment to treat subfoveal **choroidal neovascularization** (CNV). An anti-**angiogenic** drug (such as inhibitors of protein kinase C or VEGF) is used with photosensitizers (such as N-benzoylstaurosporine) for combination chemo- and photodynamic treatment of CNV.

ST **neovascularization** photodynamic therapy **angiogenesis** inhibitor combination

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor κB), inhibitors; treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)

IT **Eye**
(**choroid**; treatment of subfoveal **choroidal neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)

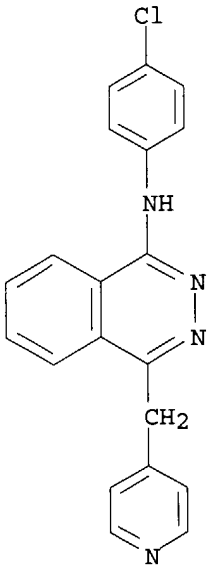
IT **Angiogenesis**
(**neovascularization**; treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)

IT Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)

IT **Angiogenesis** inhibitors
Photodynamic therapy
Photosensitizers (pharmaceutical)
(treatment of subfoveal **choroidal neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)

IT 9001-84-7, Phospholipase A2 9002-72-6, growth hormone 11128-99-7, angiotensin II 67763-96-6, IGF-1 127464-60-2, Vascular endothelial

growth factor 141436-78-4, Protein kinase C 329900-75-6, cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)
IT 75775-33-6D, Purpurin, derivs. 83150-76-9, Octreotide 120685-11-2, N-Benzoylstaurosporine **212141-54-3**, **CGP 79787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)
IT **212141-54-3**, **CGP 79787**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of **neovascularization** with combination of **angiogenesis** inhibitors and photodynamic therapy)
RN 212141-54-3 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:573541 HCAPLUS
DN 135:147425
ED Entered STN: 08 Aug 2001
TI Method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments
IN Brazzell, Romulus Kimbro; Wood, Jeanette Marjorie; **Campochiaro, Peter Anthony**; Kane, Frances Elizabeth
PA Ciba Vision Corp., USA
SO U.S., 19 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A01N043-58
NCL 514249000
CC 1-8 (Pharmacology)
Section cross-reference(s): 28
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6271233	B1	20010807	US 1999-371746	19990810 <--

PRAI US 1999-371746 19990810 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6271233	ICM	A01N043-58
	NCL	514249000

OS MARPAT 135:147425

AB The invention relates to the use of certain phthalazines in the preparation of medicaments for the treatment of **ocular neovascularization.**

ST phthalazine **ocular neovascular** disease treatment

IT **Eye**
(**choroid, neovascularization**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**diabetic retinopathy**, proliferative; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT Vascular endothelial growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene KDR; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT Vascular endothelial growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene flt 1; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**macula, senile degeneration**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Angiogenesis** inhibitors
Signal transduction, biological
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT Hepatocyte growth factor receptors
c-Kit (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Angiogenesis**
(**neovascularization, eye**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Angiogenesis**
(**neovascularization, retinal**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**neovascularization**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**retina, ischemia, retinopathy** from;

method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**retina, neovascularization**; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **Eye, disease**
(**retinopathy**, ischemic; method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **212141-51-0P 212141-52-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT **212141-57-6 212141-58-7 212141-59-8**
212141-60-1 212141-64-5 212141-66-7
212141-67-8 212141-68-9 212141-69-0
212141-70-3 212141-72-5 212141-73-6
212141-74-7 212141-75-8 212141-88-3
212141-91-8 212141-92-9 212142-18-2, CGP 79787D **212142-81-9 212142-82-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT 79079-06-4, EGF receptor kinase 127464-60-2, Vascular endothelial growth factor 136396-12-8, PDGF-receptor β kinase 137632-03-2, c-Met receptor tyrosine kinase 138359-29-2, c-Kit kinase 141350-03-0, Flt-1 VEGF receptor tyrosine kinase 144697-17-6, C-Scr receptor tyrosine kinase 145539-88-4, V-Abl tyrosine kinase 148047-29-4, Tie-2 kinase 150977-45-0, Flk-1/KDR VEGF receptor tyrosine kinase 208996-51-4, FGF-1 receptor kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

IT 106-47-8, 4-Chloroaniline, reactions 20265-96-7, 4-Chloroaniline hydrochloride **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

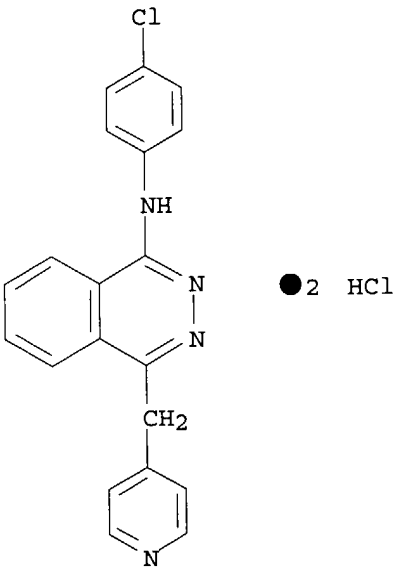
RE

(1) Anon; JP 03106875 A2 1991 HCAPLUS
(2) Anon; WO 9734876 1997 HCAPLUS
(3) Anon; WO 9734920 1997 HCAPLUS
(4) Anon; WO 9740831 1997 HCAPLUS
(5) Anon; WO 9835958 1998 HCAPLUS
(6) Anon; European Patent Office Standard Search Report
(7) Germany Needs Interdisciplinary Approach To Cancer Research; The 23rd German Cancer conference, International Cancer News 1998, P1474
(8) Hidehiro, I; Protein Kinase C Activation and Its Role in the Development of Vascular Compliclations in Diabetes Mellitus, Pharmazeutische Zeitung 1998, V34, P1474
(9) Parsons; 1965 HCAPLUS

(10) Wood, J; Proceedings of the American Association for Cancer Research 1998, V39, P96

IT **212141-51-0P 212141-52-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

RN 212141-51-0 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



RN 212141-52-1 HCAPLUS
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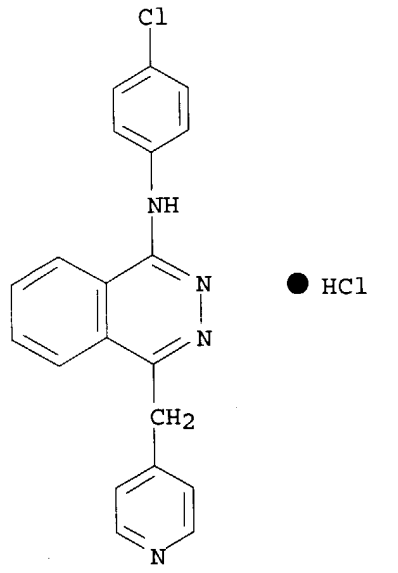

IT **212141-57-6 212141-58-7 212141-59-8**
212141-60-1 212141-64-5 212141-66-7
212141-67-8 212141-68-9 212141-69-0
212141-70-3 212141-72-5 212141-73-6
212141-74-7 212141-75-8 212141-88-3
212141-91-8 212141-92-9 212142-18-2, CGP 79787D **212142-81-9 212142-82-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)

RN 212141-57-6 HCAPLUS
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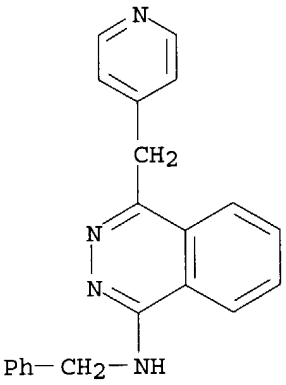
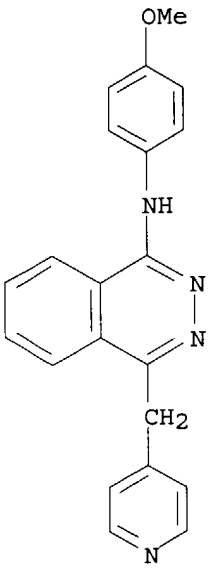


RN 212141-58-7 HCAPLUS
CN 1-Phthalazinamine, N-(4-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-59-8 HCAPLUS
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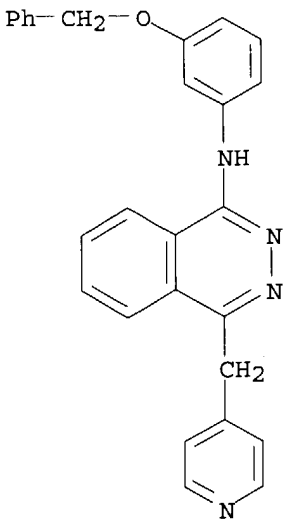
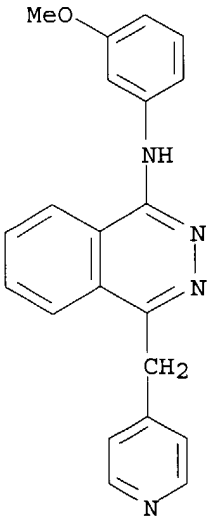
(9CI) (CA INDEX NAME)



RN 212141-60-1 HCAPLUS
CN 1-Phthalazinamine, N-(3-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



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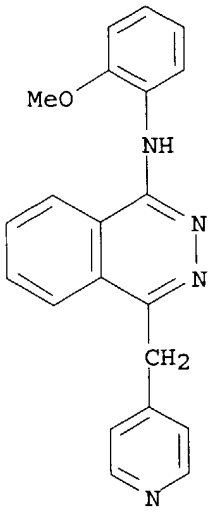
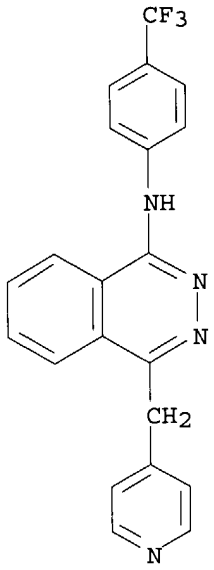


RN 212141-66-7 HCAPLUS
CN 1-Phthalazinamine, 4-(4-pyridinylmethyl)-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 212141-67-8 HCAPLUS
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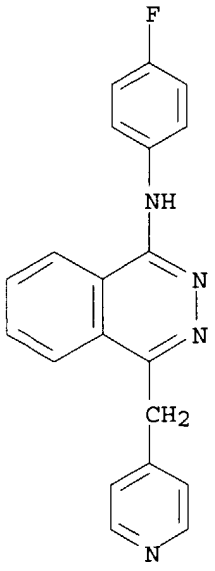
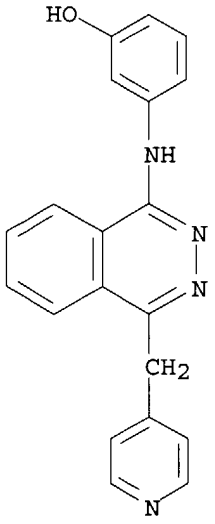
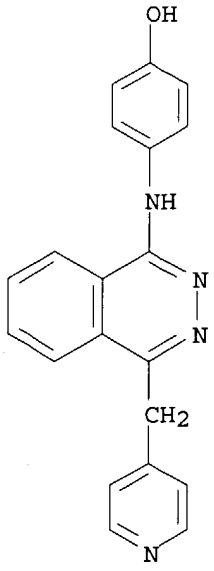


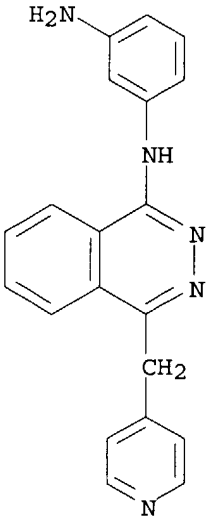
RN 212141-68-9 HCAPLUS
CN Phenol, 3-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



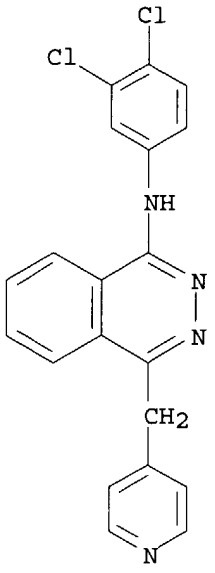
RN 212141-69-0 HCAPLUS
CN Phenol, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



RN 212141-70-3 HCAPLUS
CN 1,3-Benzenediamine, N-[4-(4-pyridinylmethyl)-1-phthalazinyl]- (9CI) (CA INDEX NAME)



RN 212141-72-5 HCAPLUS
CN 1-Phthalazinamine, N-(3,4-dichlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



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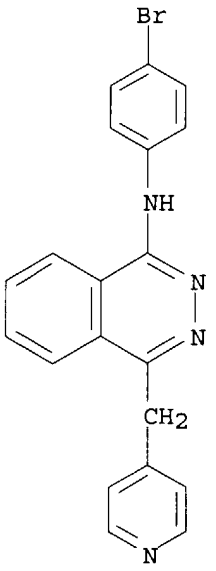
CN 1-Phthalazinamine, N-(4-bromophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



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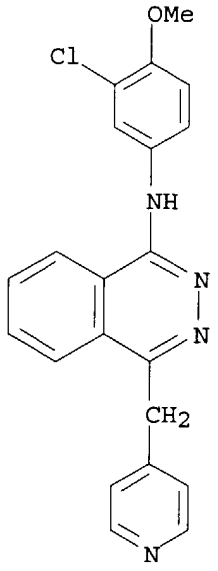
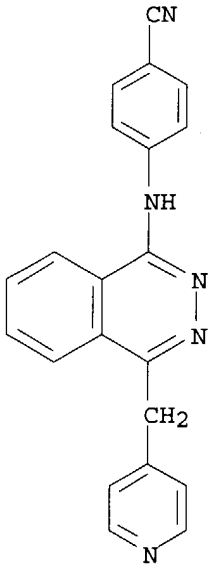


RN 212141-75-8 HCAPLUS
CN Benzonitrile, 4-[[4-(4-pyridinylmethyl)-1-phthalazinyl]amino]- (9CI) (CA INDEX NAME)



RN 212141-88-3 HCAPLUS
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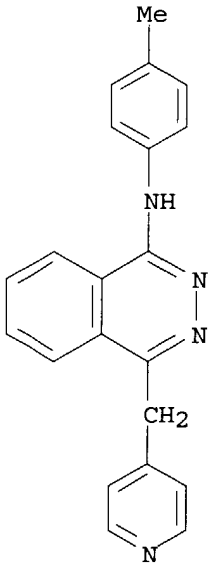

RN 212141-91-8 HCAPLUS
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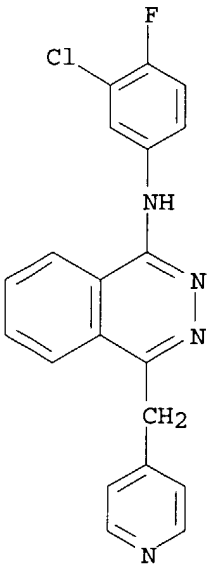

RN 212141-92-9 HCAPLUS
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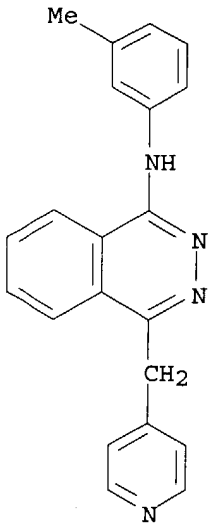
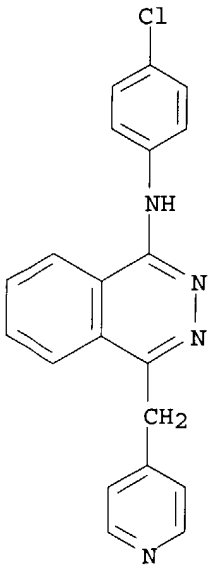


RN 212142-18-2 HCAPLUS
CN Butanedioic acid, compd. with N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-1-phthalazinamine (1:1) (9CI) (CA INDEX NAME)

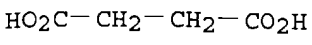
CM 1

CRN 212141-54-3
CMF C20 H15 Cl N4

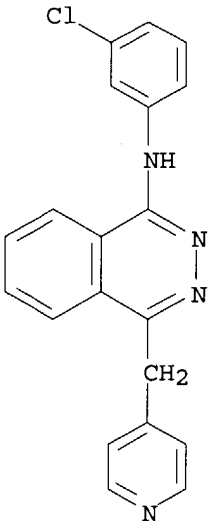


CM 2

CRN 110-15-6
CMF C4 H6 O4



RN 212142-81-9 HCAPLUS
CN 1-Phthalazinamine, N-(3-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212142-82-0 HCAPLUS
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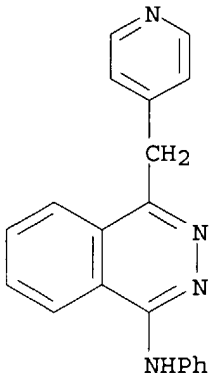
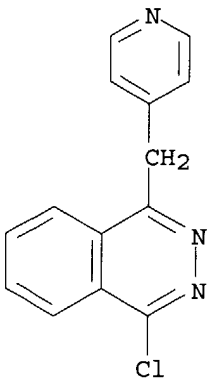
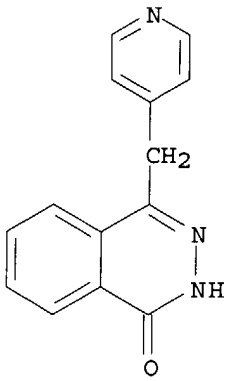


IT **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for treating **ocular neovascular** diseases using phthalazines in preparation of medicaments in relation to blockade of VEGF signaling)
RN 101094-85-3 HCAPLUS
CN Phthalazine, 1-chloro-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 107558-48-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L80 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:135394 HCAPLUS
DN 133:72358
ED Entered STN: 28 Feb 2000
TI Blockade of vascular endothelial cell growth factor receptor signaling is sufficient to completely prevent **retinal neovascularization**
AU Ozaki, Hiroaki; Seo, Man-Seong; Ozaki, Keiko; Yamada, Haruhiko; Yamada, Eri; Okamoto, Naoyuki; Hofmann, Francesco; Wood, Jeanette M.; **Campochiaro, Peter A.**
CS Department of Ophthalmology and Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
SO American Journal of Pathology (**2000**), 156(2), 696-707
CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB **Retinal** vasculogenesis and ischemic **retinopathies** provide good model systems for study of vascular development and **neovascularization** (NV), resp. Vascular endothelial cell growth factor (VEGF) has been implicated in the pathogenesis of **retinal** vasculogenesis and in the development of **retinal** NV in ischemic **retinopathies.** However, insulin-like growth factor-I and possibly

other growth factors also participate in the development of **retinal** NV and **intraocular** injections of VEGF antagonists only partially inhibit **retinal** NV. One possible conclusion from these studies is that it is necessary to block other growth factors in addition to VEGF to achieve complete inhibition of **retinal** NV. We recently demonstrated that a partially selective kinase inhibitor, PKC412, that blocks phosphorylation by VEGF and platelet-derived growth factor (PDGF) receptors and several isoforms of protein kinase C (PKC), completely inhibits **retinal** NV. In this study, we have used three addnl. selective kinase inhibitors with different selectivity profiles to explore the signaling pathways involved in **retinal** NV. **PTK787**, a drug that blocks phosphorylation by VEGF and PDGF receptors, but not PKC, completely inhibited **retinal** NV in murine oxygen-induced ischemic **retinopathy** and partially inhibited **retinal** vascularization during development. CGP 57148 and CGP 53716, two drugs that block phosphorylation by PDGF receptors, but not VEGF receptors, had no significant effect on **retinal** NV. These data and our previously published study suggest that regardless of contributions by other growth factors, VEGF signaling plays a critical role in the pathogenesis of **retinal** NV. Inhibition of VEGF receptor kinase activity completely blocks **retinal** NV and is an excellent target for treatment of proliferative **diabetic retinopathy** and other ischemic **retinopathies.**

ST VEGF PDGF receptor signaling **eye retina** **neovascularization**

IT Development, mammalian postnatal
Phosphorylation, biological
Signal transduction, biological
(VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal** **neovascularization**)

IT Platelet-derived growth factor receptors
Vascular endothelial growth factor receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal** **neovascularization**)

IT Macrophage colony-stimulating factor receptors
c-Kit (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal** **neovascularization**)

IT Vascular endothelial growth factor receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(gene KDR; VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT **Eye, disease**
(ischemic **retinopathy**; VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT **Angiogenesis**
(**neovascularization**; VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT **Eye**
(**retina**; VEGF and/or PDGF receptor tyrosine kinases role in

signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT **Eye, disease**
(**retinopathy**, ischemic; VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT 150977-45-0, FLK-1/KDR VEGF RECEPTOR TYROSINE KINASE
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

IT 80449-02-1, Tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VEGF and/or PDGF receptor tyrosine kinases role in signaling pathways in **retinal** vascular development and pathol. **retinal neovascularization**)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Adamis, A; Arch Ophthalmol 1996, V114, P66 HCAPLUS
(3) Aiello, L; N Engl J Med 1994, V331, P1480 MEDLINE
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(24) Tobe, T; Invest Ophthalmol Vis Sci 1998, V39, P180 MEDLINE
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L80 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:133467 HCAPLUS
DN 132:175828
ED Entered STN: 25 Feb 2000
TI Method using phthalazine derivatives for treating **ocular neovascular** diseases
IN Brazzell, Romulus Kimbro; Wood, Jeanette Marjorie; **Campochiaro, Peter Anthony**; Kane, Frances Elizabeth
PA **Novartis A.-G., Switz.**; **Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.**
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-8 (Pharmacology)

Section cross-reference(s): 28

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009098	A2	20000224	WO 1999-EP5876	19990811 <--
	WO 2000009098	A3	20000518		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9957330	A1	20000306	AU 1999-57330	19990811 <--
	EP 1105136	A2	20010613	EP 1999-944371	19990811 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522475	T2	20020723	JP 2000-564601	19990811 <--
	US 6214819	B1	20010410	US 1999-442781	19991118 <--
PRAI	US 1998-133855	A	19980813 <--		
	WO 1999-EP5876	W	19990811 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000009098	ICM	A61K031-00

OS MARPAT 132:175828

AB Phthalazines are used in the preparation of medicaments for the treatment of **ocular neovascularization.**

ST phthalazine deriv prepn **ocular neovascular** disease

IT **Eye, disease**
(**diabetic retinopathy**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Eye, disease**
(**macula, senile degeneration**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Angiogenesis**
Angiogenesis
(**neovascularization, eye**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Angiogenesis**
(**neovascularization, retinal**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Eye, disease**
(**neovascularization**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Angiogenesis** inhibitors
(phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Eye, disease**
(**retinopathy**, ischemic; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **Eye, disease**
(**retinopathy, neovascularization**; phthalazine derivs. for treating **ocular neovascular** diseases)

IT 152459-94-4, CGP 53716 152459-95-5, CGP 57148
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(phthalazine derivs. for treating **ocular neovascular** diseases)

IT **212141-51-0P 212141-52-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phthalazine derivs. for treating **ocular neovascular** diseases)

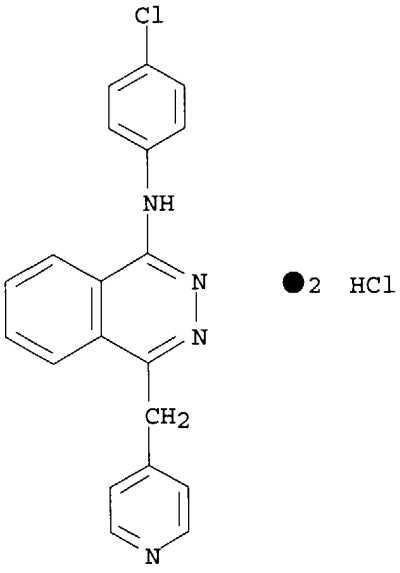
IT 253-52-1D, Phthalazine, derivs. **212141-54-3**, CGP 79787D **212141-57-6 212141-58-7 212141-59-8 212141-60-1 212141-64-5 212141-66-7 212141-67-8 212141-68-9 212141-69-0 212141-70-3 212141-72-5 212141-73-6 212141-74-7 212141-75-8 212141-88-3 212141-91-8 212141-92-9 212142-81-9 212142-82-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phthalazine derivs. for treating **ocular neovascular** diseases)

IT 79079-06-4, EGF receptor kinase 127464-60-2, Vascular endothelial growth factor 137632-03-2, c-Met receptor tyrosine kinase 138359-29-2, c-Kit kinase 141350-03-0, Flt1 receptor tyrosine kinase 144697-17-6, C-Scr receptor tyrosine kinase 145539-88-4, v-Abl tyrosine kinase 148047-29-4, Tie-2 kinase 150027-21-7, PDGF-RA receptor tyrosine kinase 150977-45-0, Kdr receptor tyrosine kinase 150977-45-0, Flk-1 receptor tyrosine kinase 208996-51-4, FGF-1 receptor kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(phthalazine derivs. for treating **ocular neovascular** diseases)

IT 106-47-8, 4-Chloroaniline, reactions 20265-96-7, 4-Chloroaniline hydrochloride **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; phthalazine derivs. for treating **ocular neovascular** diseases)

IT **212141-51-0P 212141-52-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phthalazine derivs. for treating **ocular neovascular** diseases)

RN 212141-51-0 HCAPLUS
CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



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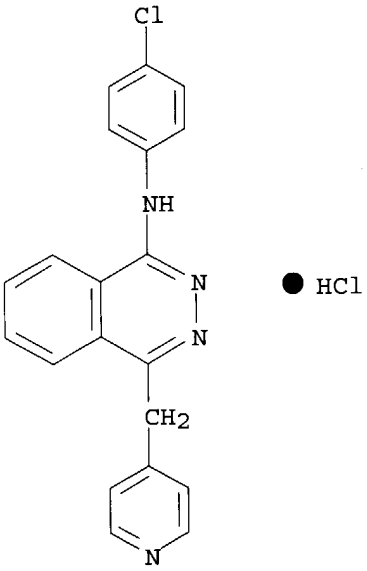

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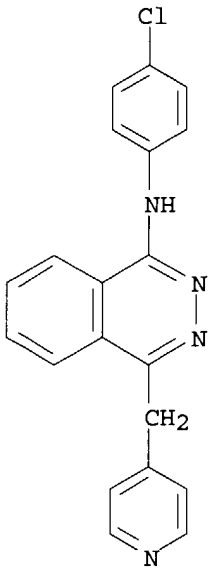
212141-69-0 212141-70-3 212141-72-5
212141-73-6 212141-74-7 212141-75-8
212141-88-3 212141-91-8 212141-92-9
212142-81-9 212142-82-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phthalazine derivs. for treating **ocular neovascular** diseases)

RN 212141-54-3 HCAPLUS

CN 1-Phthalazinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-57-6 HCAPLUS
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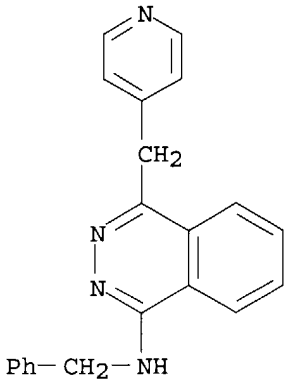

RN 212141-58-7 HCAPLUS
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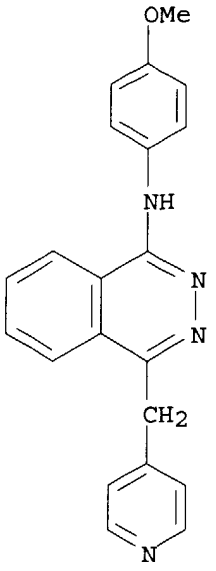
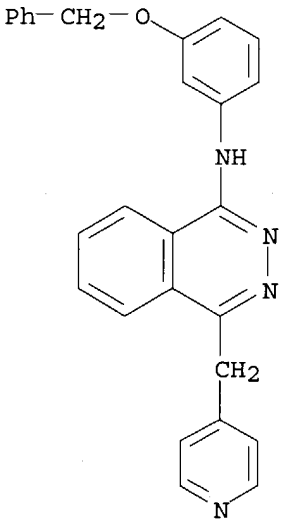
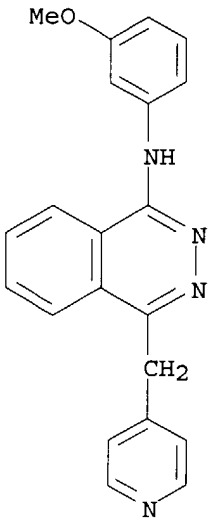


RN 212141-59-8 HCAPLUS
CN 1-Phthalazinamine, N-[3-(phenylmethoxy)phenyl]-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 212141-60-1 HCAPLUS
CN 1-Phthalazinamine, N-(3-methoxyphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



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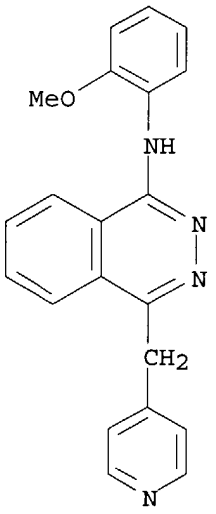

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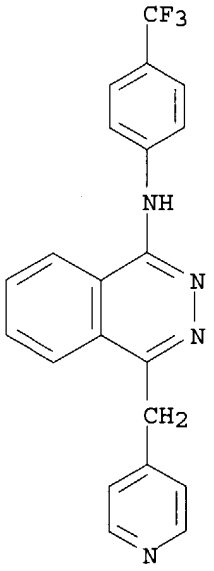

RN 212141-67-8 HCAPLUS
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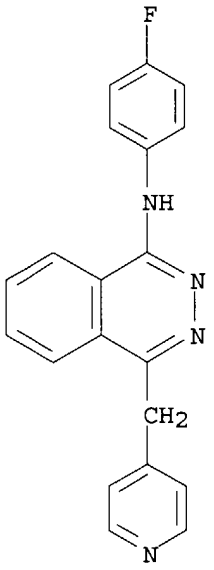

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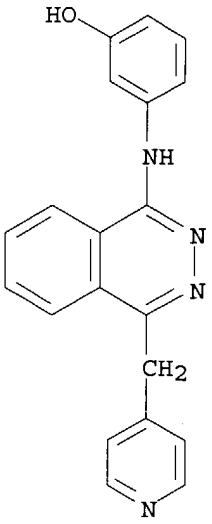

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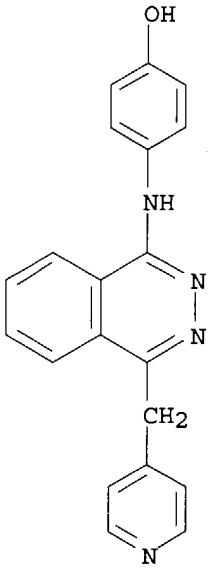

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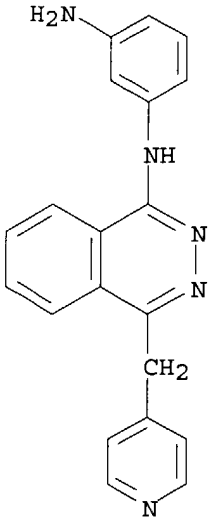

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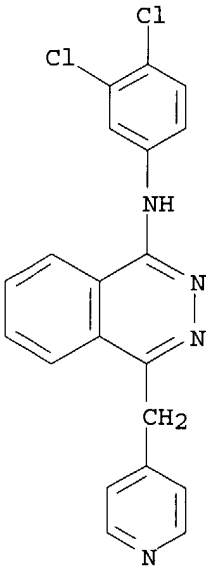

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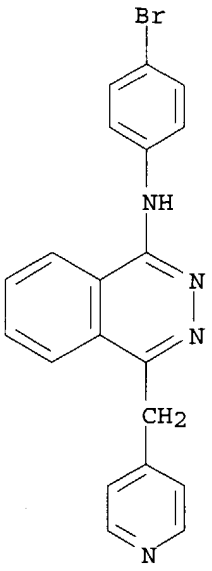

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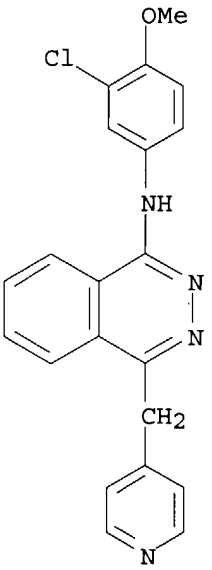

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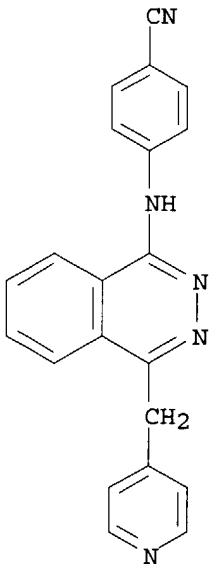

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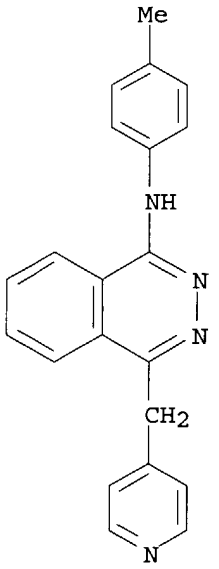

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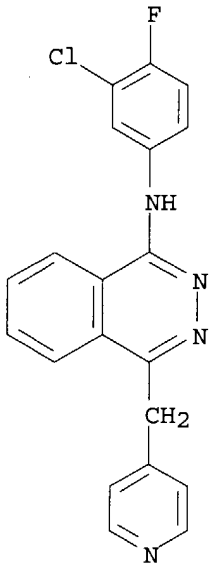

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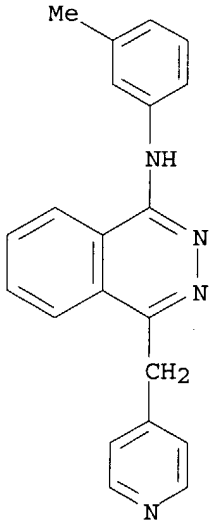

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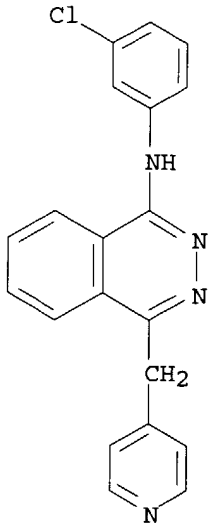

RN 212142-82-0 HCAPLUS
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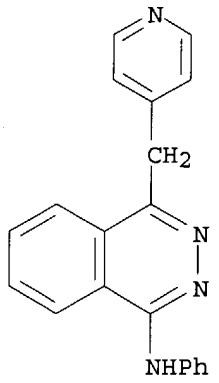
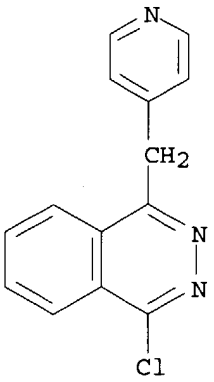
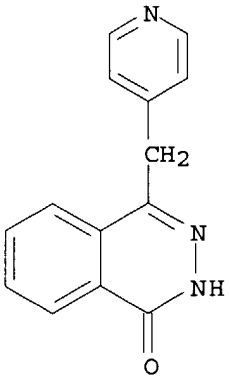


IT **101094-85-3 107558-48-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; phthalazine derivs. for treating **ocular neovascular** diseases)
RN 101094-85-3 HCAPLUS
CN Phthalazine, 1-chloro-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 107558-48-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



=> => fil biosis
FILE 'BIOSIS' ENTERED AT 07:14:43 ON 13 OCT 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 October 2004 (20041006/ED)

FILE RELOADED: 19 October 2003.

=> d all tot

L90 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:465239 BIOSIS
DN PREV200200465239
TI CGP 79787D (**PTK787**/ZK222584), CGP 84738, NVP-AAC789, NVP-AAD777 and related 1-anilino-(4-pyridylmethyl)phthalazines as inhibitors of VEGF- and bFGF-induced angiogenesis.
AU Bold, Guido [Reprint author]; Frei, Jorg; Furet, Pascal; Manley, Paul W.; Bruggen, Josef; Cozens, Robert; Ferrari, Stefano; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Jurgen; Meyer, Thomas; Wood, Jeanette M.
CS Novartis Pharma AG, K-136.4.82, CH-4057, Basel, Switzerland

SO Drugs of the Future, (January, 2002) Vol. 27, No. 1, pp. 43-55. print.
ISSN: 0377-8282.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 4 Sep 2002
Last Updated on STN: 4 Sep 2002
CC Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
Cardiovascular system - Physiology and biochemistry 14504
Cardiovascular system - Blood vessel pathology 14508
Endocrine - General 17002
Endocrine - Pancreas 17008
Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Sense organs - Pathology 20006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Cardiovascular system 22010
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Immunology - Immunopathology, tissue immunology 34508
Allergy 35500
IT Major Concepts
Cardiovascular System (Transport and Circulation); Pharmacology; Tumor Biology
IT Parts, Structures, & Systems of Organisms
tumor cells
IT Diseases
cancer: neoplastic disease
Neoplasms (MeSH)
IT Diseases
diabetic retinopathy: endocrine disease/pancreas, eye disease, metabolic disease, vascular disease
Diabetic **Retinopathy** (MeSH)
IT Diseases
macular degeneration: eye disease
Macular Degeneration (MeSH)
IT Diseases
metastasis: neoplastic disease
IT Diseases
rheumatoid arthritis: connective tissue disease, immune system disease, joint disease
Arthritis, Rheumatoid (MeSH)
IT Chemicals & Biochemicals
1-anilino-(4-pyridylmethyl)phthalazines: cardiovascular-drug, angiogenesis inhibitor, oral administration; CGP 84738: cardiovascular-drug, angiogenesis inhibitor; CPG 79787D [**PTK787** /ZK222584]: antiangiogenesis drug; NVP-AAC789: angiogenesis inhibitor; NVP-AAD777: angiogenesis inhibitor; fibroblast growth factor [FGF]: cytokine; platelet-derived growth factor [PDGF]: cytokine; vascular endothelial growth factor [VEGF]: cytokine; vascular endothelial growth factor tyrosine kinase inhibitor: enzyme inhibitor-drug, angiogenesis modulator
IT Methods & Equipment
antiangiogenesis therapy: therapeutic method
IT Miscellaneous Descriptors
angiogenesis; neovascularization; tumor growth
ORGN Classifier
Hominidae 86215
Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line: human umbilical vein endothelial cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 62031-54-3 (fibroblast growth factor)
62031-54-3 (FGF)
127464-60-2 (vascular endothelial growth factor)
127464-60-2 (VEGF)

L90 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN **2000:347636** BIOSIS
DN **PREV200000347636**
TI Blockade of vascular endothelial cell growth factor receptor signaling is sufficient to completely prevent **retinal neovascularization.**
AU Ozaki, Hiroaki; Seo, Man-Seong; Ozaki, Keiko; Yamada, Haruhiko; Yamada, Eri; Okamoto, Naoyuki; Hofmann, Francesco; Wood, Jeanette M.; Campochiaro, Peter A. [Reprint author]
CS The Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Maumenee 719, Baltimore, MD, 21287-9277, USA
SO American Journal of Pathology, (February, 2000) Vol. 156, No. 2, pp. 697-707. print.
CODEN: AJPAA4. ISSN: 0002-9440.
DT Article
LA English
ED Entered STN: 16 Aug 2000
Last Updated on STN: 7 Jan 2002
AB **Retinal** vasculogenesis and ischemic **retinopathies** provide good model systems for study of vascular development and **neovascularization** (NV), respectively. Vascular endothelial cell growth factor (VEGF) has been implicated in the pathogenesis of **retinal** vasculogenesis and in the development of **retinal** NV in ischemic **retinopathies.** However, insulin-like growth factor-I and possibly other growth factors also participate in the development of **retinal** NV and **intraocular** injections of VEGF antagonists only partially inhibit **retinal** NV. One possible conclusion from these studies is that it is necessary to block other growth factors in addition to VEGF to achieve complete inhibition of **retinal** NV. We recently demonstrated that a partially selective kinase inhibitor, PKC412, that blocks phosphorylation by VEGF and platelet-derived growth factor (PDGF) receptors and several isoforms of protein kinase C (PKC), completely inhibits **retinal** NV. In this study, we have used three additional selective kinase inhibitors with different selectivity profiles to explore the signaling pathways involved in **retinal** NV. **PTK787**, a drug that blocks phosphorylation by VEGF and PDGF receptors, but not PKC, completely inhibited **retinal** NV in murine oxygen-induced ischemic **retinopathy** and partially inhibited **retinal** vascularization during development. CGP 57148 and CGP 53716, two dru that block phosphorylation by PDGF receptors, but not VEGF receptors, no significant effect on **retinal** NV. These data and our previously published study suggest that regardless of contributions b other growth factors, VEGF signaling plays a critical role in the

pathogenesis of **retinal** NV. Inhibition of VEGF receptor kinase activity completely blocks **retinal** NV and is an excellent target for treatment of proliferative diabetic **retinopathy** and other ischemic **retinopathies.**

CC Biophysics - Membrane phenomena 10508
Cytology - Animal 02506
Enzymes - General and comparative studies: coenzymes 10802
Cardiovascular system - Physiology and biochemistry 14504
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006

IT Major Concepts
Membranes (Cell Biology); Sense Organs (Sensory Reception); Cardiovascular System (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
retina: sensory system

IT Diseases
ischemic retinopathy: eye disease

IT Chemicals & Biochemicals
PKC412: partially selective kinase inhibitor; platelet-derived growth factor receptors; protein kinase C; vascular endothelial cell growth factor

IT Miscellaneous Descriptors
neovascularization; **retinal** vasculogenesis; vascular development

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 120685-11-2 (PKC412)
141436-78-4 (protein kinase C)

=> => fil medline
FILE 'MEDLINE' ENTERED AT 07:17:10 ON 13 OCT 2004

FILE LAST UPDATED: 12 OCT 2004 (20041012/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L97 ANSWER 1 OF 2 MEDLINE on STN
AN 2000428217 MEDLINE
DN PubMed ID: 10967078
TI VEGF is major stimulator in model of choroidal neovascularization.
AU Kwak N; Okamoto N; Wood J M; Campochiaro P A
CS Departments of Ophthalmology and Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287-9277, USA.
NC EY05951 (NEI)

EY12609 (NEI)
P30EY1765 (NEI)
+
SO Investigative ophthalmology & visual science, **(2000 Sep)** 41 (10) 3158-64.
Journal code: 7703701. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

AB PURPOSE: Vascular endothelial growth factor (VEGF) is upregulated by hypoxia and is a major stimulatory factor for retinal neovascularization in ischemic retinopathies such as diabetic retinopathy. This study sought to determine if VEGF is a stimulatory factor in a murine model of choroidal neovascularization (CNV). METHODS: Mice with laser-induced ruptures in Bruch's membrane were treated with vehicle alone; a drug that inhibits both VEGF and platelet-derived growth factor (PDGF) receptor kinases; a drug that inhibits PDGF, but not VEGF receptor kinase; or genistein, a nonspecific kinase inhibitor. After two weeks, CNV was quantified and compared. RESULTS: Blockade of phosphorylation by VEGF and PDGF receptors caused dramatic, almost complete inhibition of CNV. Genistein also had an inhibitory effect, but less so than the VEGF/PDGF receptor blocker. Blockade of phosphorylation by PDGF receptors, but not VEGF receptors, had no significant effect on CNV. CONCLUSIONS: These data and our previous study, which demonstrated that a kinase inhibitor that blocks VEGF and PDGF receptors and several isoforms of protein kinase C causing dramatic inhibition of CNV, suggest that VEGF signaling plays a critical role in the development of CNV in this model. If safety is established, the effect of inhibiting VEGF receptor kinase activity should be investigated in patients with CNV.

CT Check Tags: Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Animals
***Choroidal Neovascularization: ME, metabolism**
Choroidal Neovascularization: PA, pathology
Choroidal Neovascularization: PC, prevention & control
*Endothelial Growth Factors: PH, physiology
Enzyme Inhibitors: PD, pharmacology
Genistein: PD, pharmacology
*Lymphokines: PH, physiology
Mice
Mice, Inbred C57BL
Phosphorylation
Phthalazines: PD, pharmacology
Platelet-Derived Growth Factor: PH, physiology
Protein Kinase C: AI, antagonists & inhibitors
Pyridines: PD, pharmacology
Pyrimidines: PD, pharmacology
Receptor Protein-Tyrosine Kinases: AI, antagonists & inhibitors
Receptors, Growth Factor: AI, antagonists & inhibitors
Receptors, Platelet-Derived Growth Factor: AI, antagonists & inhibitors
Receptors, Vascular Endothelial Growth Factor
Signal Transduction: PH, physiology
Vascular Endothelial Growth Factor A
Vascular Endothelial Growth Factors
RN **212142-18-2 (vatalanib)**; 446-72-0 (Genistein)
CN 0 (CGP 53716); 0 (Endothelial Growth Factors); 0 (Enzyme Inhibitors); 0 (Lymphokines); 0 (Phthalazines); 0 (Platelet-Derived Growth Factor); 0 (Pyridines); 0 (Pyrimidines); 0 (Receptors, Growth Factor); 0 (Vascular Endothelial Growth Factor A); 0 (Vascular Endothelial Growth Factors); EC

2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptors, Platelet-Derived Growth Factor); EC 2.7.1.112 (Receptors, Vascular Endothelial Growth Factor); EC 2.7.1.37 (Protein Kinase C)

L97 ANSWER 2 OF 2 MEDLINE on STN
AN 2000132839 MEDLINE
DN PubMed ID: 10666398
TI Blockade of vascular endothelial cell growth factor receptor signaling is sufficient to completely prevent **retinal** neovascularization.
AU Ozaki H; Seo M S; Ozaki K; Yamada H; Yamada E; Okamoto N; Hofmann F; Wood J M; Campochiaro P A
CS Department of Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
NC EY05951 (NEI)
P30EY1765 (NEI)
SO American journal of pathology, **(2000 Feb)** 156 (2) 697-707.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200003
ED Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309
AB **Retinal** vasculogenesis and ischemic **retinopathies** provide good model systems for study of vascular development and neovascularization (NV), respectively. Vascular endothelial cell growth factor (VEGF) has been implicated in the pathogenesis of **retinal** vasculogenesis and in the development of **retinal** NV in ischemic **retinopathies.** However, insulin-like growth factor-I and possibly other growth factors also participate in the development of **retinal** NV and intraocular injections of VEGF antagonists only partially inhibit **retinal** NV. One possible conclusion from these studies is that it is necessary to block other growth factors in addition to VEGF to achieve complete inhibition of **retinal** NV. We recently demonstrated that a partially selective kinase inhibitor, PKC412, that blocks phosphorylation by VEGF and platelet-derived growth factor (PDGF) receptors and several isoforms of protein kinase C (PKC), completely inhibits **retinal** NV. In this study, we have used three additional selective kinase inhibitors with different selectivity profiles to explore the signaling pathways involved in **retinal** NV. **PTK787**, a drug that blocks phosphorylation by VEGF and PDGF receptors, but not PKC, completely inhibited **retinal** NV in murine oxygen-induced ischemic **retinopathy** and partially inhibited **retinal** vascularization during development. CGP 57148 and CGP 53716, two drugs that block phosphorylation by PDGF receptors, but not VEGF receptors, had no significant effect on **retinal** NV. These data and our previously published study suggest that regardless of contributions by other growth factors, VEGF signaling plays a critical role in the pathogenesis of **retinal** NV. Inhibition of VEGF receptor kinase activity completely blocks **retinal** NV and is an excellent target for treatment of proliferative diabetic **retinopathy** and other ischemic **retinopathies.**
CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Aging: PH, physiology
Angiogenesis Inhibitors: PD, pharmacology
Animals
Animals, Newborn: GD, growth & development
Animals, Newborn: PH, physiology
Endothelial Growth Factors: GE, genetics
Enzyme Inhibitors: PD, pharmacology
Ischemia: CO, complications

Ischemia: PA, pathology
Lymphokines: GE, genetics
Mice
Mice, Inbred C57BL
Mice, Transgenic: GE, genetics
Mice, Transgenic: PH, physiology
Neovascularization, Pathologic: PA, pathology
*Neovascularization, Pathologic: PP, physiopathology
Neovascularization, Pathologic: PC, prevention & control
Phosphotransferases: AI, antagonists & inhibitors
*Phthalazines
Receptor Protein-Tyrosine Kinases: AI, antagonists & inhibitors
*Receptor Protein-Tyrosine Kinases: PH, physiology
Receptors, Growth Factor: AI, antagonists & inhibitors
*Receptors, Growth Factor: PH, physiology
Receptors, Vascular Endothelial Growth Factor
Retinal Vessels: DE, drug effects
Retinal Vessels: GD, growth & development
Retinal Vessels: PA, pathology
***Retinal Vessels: PP, physiopathology**
Rhodopsin: GE, genetics
*Signal Transduction: PH, physiology
Vascular Endothelial Growth Factor A
Vascular Endothelial Growth Factors
RN **212142-18-2 (vatalanib)**; 9009-81-8 (Rhodopsin)
CN 0 (Angiogenesis Inhibitors); 0 (Endothelial Growth Factors); 0 (Enzyme Inhibitors); 0 (Lymphokines); 0 (Phthalazines); 0 (Receptors, Growth Factor); 0 (Vascular Endothelial Growth Factor A); 0 (Vascular Endothelial Growth Factors); EC 2.7 (Phosphotransferases); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptors, Vascular Endothelial Growth Factor)

=> => fil embase
FILE 'EMBASE' ENTERED AT 07:19:17 ON 13 OCT 2004

FILE COVERS 1974 TO 7 Oct 2004 (20041007/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L101 ANSWER 1 OF 8 EMBASE
on STN
AN 2002458200 EMBASE
TI Therapies directed at vascular endothelial growth factor.
AU Manley P.W.; Martiny-Baron G.; Schlaeppi J.-M.; Wood J.M.
CS P.W. Manley, Novartis Pharma Ltd., CH-4057 Basel, Switzerland
SO Expert Opinion on Investigational Drugs, (1 Dec 2002) 11/12 (1715-1736).
Refs: 199
ISSN: 1354-3784 CODEN: EOIDER
CY United Kingdom
DT Journal; General Review
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LA English
SL English
AB The inhibition of angiogenesis through vascular endothelial growth factor (VEGF) receptor targeting is a strategy that is relatively tumour selective. The high selectivity achieved with neutralising antibodies, soluble receptors and ribozymes reduces the risk of adverse reactions not related to VEGF inhibition itself. Small-molecule, orally-active protein kinase inhibitors provide an attractive alternative for chronic therapy, although specifically targeting a small subset of protein kinases from the .apprx. 550 expressed in mammalian cells is a challenge. Current efforts have resulted in promising clinical data for several synthetic VEGF receptor kinase inhibitors, of which **PTK787**/ZK222584 and ZD6474 are proceeding into large size clinical trials. It seems likely that blockers of the VEGF signalling pathway will be unsuitable for monotherapy, and that their role will be as an adjunct to additional antiangiogenic agents together with directly-acting antitumour agents or radiation therapy. Caution is needed with combinations of antiVEGF therapies and cytotoxic agents, as coadministration of cytotoxic agents with either the kinase inhibitor SU5416 or the VEGF antibody avastin appears to be associated with bleeding and thrombotic adverse events.
CT Medical Descriptors:
drug targeting
angiogenesis
inhibition kinetics
drug selectivity
protein expression
mammal cell
signal transduction
monotherapy
cancer radiotherapy
bleeding: SI, side effect
thrombosis: SI, side effect
pathophysiology
malignant neoplastic disease
rheumatoid arthritis
eye disease
psoriasis
breast cancer: DT, drug therapy
colorectal cancer: DT, drug therapy
lung cancer: DT, drug therapy
drug half life
diarrhea: SI, side effect
thrombocytopenia: SI, side effect
lung non small cell cancer: DT, drug therapy
drug structure
human
nonhuman
mouse
clinical trial
review
Drug Descriptors:
*vasculotropin: EC, endogenous compound
*vasculotropin inhibitor: AE, adverse drug reaction
*vasculotropin inhibitor: CT, clinical trial
*vasculotropin inhibitor: AN, drug analysis
*vasculotropin inhibitor: CB, drug combination
*vasculotropin inhibitor: CM, drug comparison
*vasculotropin inhibitor: DV, drug development
*vasculotropin inhibitor: DT, drug therapy
*vasculotropin inhibitor: PK, pharmacokinetics
*vasculotropin inhibitor: PD, pharmacology
*vasculotropin inhibitor: IP, intraperitoneal drug administration
*vasculotropin inhibitor: IV, intravenous drug administration

*vasculotropin inhibitor: SC, subcutaneous drug administration
cep 7055: CT, clinical trial
cep 7055: AN, drug analysis
cep 7055: DV, drug development
cep 7055: DT, drug therapy
cep 7055: PD, pharmacology
cp 547632: CT, clinical trial
cp 547632: DV, drug development
cp 547632: DT, drug therapy
cp 547632: PD, pharmacology
vasculotropin receptor: EC, endogenous compound
neutralizing antibody: CT, clinical trial
neutralizing antibody: DV, drug development
neutralizing antibody: DT, drug therapy
neutralizing antibody: PD, pharmacology
ribozyme: EC, endogenous compound
protein kinase inhibitor: AE, adverse drug reaction
protein kinase inhibitor: CT, clinical trial
protein kinase inhibitor: AN, drug analysis
protein kinase inhibitor: CB, drug combination
protein kinase inhibitor: CM, drug comparison
protein kinase inhibitor: DV, drug development
protein kinase inhibitor: DT, drug therapy
protein kinase inhibitor: PK, pharmacokinetics
protein kinase inhibitor: PD, pharmacology
protein kinase inhibitor: PO, oral drug administration
zd 6474: CT, clinical trial
zd 6474: AN, drug analysis
zd 6474: DV, drug development
zd 6474: DT, drug therapy
zd 6474: PD, pharmacology
protein kinase: EC, endogenous compound
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: CT, clinical trial
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: AN, drug analysis
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DV, drug development
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DT, drug therapy
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PO, oral drug administration
angiogenesis inhibitor: CB, drug combination
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CB, drug combination
antineoplastic agent: CM, drug comparison
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CB, drug combination
cytotoxic agent: DT, drug therapy
cytotoxic agent: PD, pharmacology
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: AE, adverse drug reaction
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CB, drug combination
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: IV, intravenous drug administration

vasculotropin antibody: AE, adverse drug reaction
vasculotropin antibody: CT, clinical trial
vasculotropin antibody: CB, drug combination
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology
vasculotropin antibody: IP, intraperitoneal drug administration
vasculotropin receptor 1: EC, endogenous compound
vasculotropin receptor 2: EC, endogenous compound
vasculotropin receptor 3: EC, endogenous compound
neuropilin 1: EC, endogenous compound
neuropilin 2: EC, endogenous compound
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: CM, drug comparison
bevacizumab: DV, drug development
bevacizumab: DT, drug therapy
bevacizumab: PK, pharmacokinetics
bevacizumab: PD, pharmacology
doxorubicin: CB, drug combination
doxorubicin: CM, drug comparison
doxorubicin: DT, drug therapy
doxorubicin: PD, pharmacology
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: CM, drug comparison
fluorouracil: DT, drug therapy
fluorouracil: PD, pharmacology
folinic acid: CT, clinical trial
folinic acid: CB, drug combination
folinic acid: CM, drug comparison
folinic acid: DT, drug therapy
folinic acid: PD, pharmacology
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: CM, drug comparison
carboplatin: DT, drug therapy
carboplatin: PD, pharmacology
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: CM, drug comparison
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
vinblastine: CB, drug combination
vinblastine: CM, drug comparison
vinblastine: PD, pharmacology
angiozyme: AE, adverse drug reaction
angiozyme: CT, clinical trial
angiozyme: DV, drug development
angiozyme: DT, drug therapy
angiozyme: PK, pharmacokinetics
angiozyme: PD, pharmacology
angiozyme: IV, intravenous drug administration
angiozyme: SC, subcutaneous drug administration
unindexed drug
unclassified drug
rpi 4610
angioyzme

RN (vasculotropin) 127464-60-2; (vasculotropin receptor) 301253-48-5; (protein kinase) 9026-43-1; (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine) **212142-18-2**; (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (neuropilin 1) 214210-47-6, 339035-30-2; (neuropilin 2) 227018-38-4;

(bevacizumab) 216974-75-3; (doxorubicin) 23214-92-8, 25316-40-9; (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2; (carboplatin) 41575-94-4; (paclitaxel) 33069-62-4; (vinblastine) 865-21-4

CN **(1) Ptk 787**; (2) Zk 222584; (3) Zd 6474; (4) Su 5416; (5) Avastin; (6) Rpi 4610; (7) Angioyzme; (8) Angioyzme; (9) Rpi 4610; **(10) Ptk 787**; (11) Zk 222584; (12) Cep 7055; (13) Cep 7055; (14) Cp 547632

CO (2) Novartis; (3) Astra Zeneca; (4) Pharmacia; (5) Genentech; (7) Chiron; (9) Ribozyme Pharmaceuticals; (11) Schering; (12) Cephalon; (13) Sanofi Synthelabo; (14) Pfizer; Protein Design; Imclone; Merck Sharp and Dohme

L101 ANSWER 2 OF 8 EMBASE
on STN

AN 2002240091 EMBASE

TI The use of computational methods in the discovery and design of kinase inhibitors.

AU Woolfrey J.R.; Weston G.S.

CS J.R. Woolfrey, Millennium Pharmaceuticals Inc., 256 East Grand Avenue, South San Francisco, CA 94080, United States. john.woolfrey@mpi.com

SO Current Pharmaceutical Design, (2002) 8/17 (1527-1545).
Refs: 96
ISSN: 1381-6128 CODEN: CPDEFP

CY Netherlands

DT Journal; General Review

FS 016 Cancer
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LA English

SL English

AB The recent success of the first FDA-approved small-molecule tyrosine kinase inhibitor Gleevec® (STI-571, imatinib mesylate) in the treatment of chronic myelogenous leukemia (CML) has focused attention on the potential therapeutic usefulness of inhibitors of other kinase targets. This review shall highlight recent applications of computational chemistry methods, comprising both ligand-based and structure-based approaches, in the discovery and design of kinase inhibitors. In particular, we will focus on ATP-competitive inhibitors of selected kinase targets of therapeutic importance.

CT Medical Descriptors:
methodology
drug design
chronic myeloid leukemia: DT, drug therapy
enzyme structure
competitive inhibition
drug targeting
breast cancer: DT, drug therapy
drug structure
quantitative structure activity relation
drug receptor binding
diabetic retinopathy: DT, drug therapy
drug potency
drug selectivity
human
nonhuman
controlled study
review
priority journal
Drug Descriptors:
*protein kinase inhibitor: AN, drug analysis
*protein kinase inhibitor: CM, drug comparison
*protein kinase inhibitor: DV, drug development
*protein kinase inhibitor: DT, drug therapy

*protein kinase inhibitor: PD, pharmacology
*protein kinase: EC, endogenous compound
ligand: AN, drug analysis
ligand: CM, drug comparison
ligand: DV, drug development
ligand: DT, drug therapy
ligand: PD, pharmacology
protein tyrosine kinase inhibitor: AN, drug analysis
protein tyrosine kinase inhibitor: CM, drug comparison
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
imatinib: AN, drug analysis
imatinib: DT, drug therapy
imatinib: PD, pharmacology
adenosine triphosphate: EC, endogenous compound
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
protein tyrosine kinase: EC, endogenous compound
protein serine threonine kinase: EC, endogenous compound
epidermal growth factor receptor kinase: EC, endogenous compound
benzylidene derivative: AN, drug analysis
benzylidene derivative: CM, drug comparison
benzylidene derivative: DV, drug development
benzylidene derivative: PD, pharmacology
indole derivative: AN, drug analysis
indole derivative: CM, drug comparison
indole derivative: DV, drug development
indole derivative: PD, pharmacology
cyclin dependent kinase 1: EC, endogenous compound
cyclin dependent kinase 2: EC, endogenous compound
staurosporine: AN, drug analysis
staurosporine: DV, drug development
staurosporine: PD, pharmacology
purine derivative: AN, drug analysis
purine derivative: DV, drug development
purine derivative: PD, pharmacology
purvalanol B: AN, drug analysis
purvalanol B: DV, drug development
purvalanol B: PD, pharmacology
flavopiridol: AN, drug analysis
flavopiridol: DV, drug development
flavopiridol: PD, pharmacology
paullone derivative: AN, drug analysis
paullone derivative: DV, drug development
paullone derivative: PD, pharmacology
kenpaullone: AN, drug analysis
kenpaullone: DV, drug development
kenpaullone: PD, pharmacology
vasculotropin receptor 2: EC, endogenous compound
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: AN, drug analysis
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DT, drug therapy
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
protein kinase C: EC, endogenous compound
protein kinase C inhibitor: AN, drug analysis
protein kinase C inhibitor: DT, drug therapy
protein kinase C inhibitor: PD, pharmacology
9 [(dimethylamino)methyl] 6,7,10,11 tetrahydro 9h,18h 5,21:12,17
dimethenodibenzo[e,k]pyrrolo[3,4 h][1,4,13]oxadiazacyclohexadecine
18,20(19h) dione: AN, drug analysis
9 [(dimethylamino)methyl] 6,7,10,11 tetrahydro 9h,18h 5,21:12,17
dimethenodibenzo[e,k]pyrrolo[3,4 h][1,4,13]oxadiazacyclohexadecine
18,20(19h) dione: DT, drug therapy

9 [(dimethylamino)methyl] 6,7,10,11 tetrahydro 9h,18h 5,21:12,17 dimethenodibenzo[e,k]pyrrolo[3,4 h][1,4,13]oxadiazacyclohexadecine 18,20(19h) dione: PD, pharmacology
olomoucine: AN, drug analysis
olomoucine: CM, drug comparison
olomoucine: DV, drug development
olomoucine: PD, pharmacology
cyclin dependent kinase inhibitor: AN, drug analysis
cyclin dependent kinase inhibitor: DV, drug development
cyclin dependent kinase inhibitor: PD, pharmacology
2 (2 aminocyclohexylamino) 6 (3,4 dichloroanilino) 9 ethylpurine: AN, drug analysis
2 (2 aminocyclohexylamino) 6 (3,4 dichloroanilino) 9 ethylpurine: CM, drug comparison
2 (2 aminocyclohexylamino) 6 (3,4 dichloroanilino) 9 ethylpurine: DV, drug development
2 (2 aminocyclohexylamino) 6 (3,4 dichloroanilino) 9 ethylpurine: PD, pharmacology
pkf 049 365: AN, drug analysis
pkf 049 365: DV, drug development
pkf 049 365: PD, pharmacology
unindexed drug
unclassified drug

RN (protein kinase) 9026-43-1; (imatinib) 152459-95-5, 220127-57-1; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (trastuzumab) 180288-69-1; (protein tyrosine kinase) 80449-02-1; (epidermal growth factor receptor kinase) 79079-06-4; (cyclin dependent kinase 2) 141349-86-2; (staurosporine) 62996-74-1; (purvalanol B) 212844-54-7; (flavopiridol) 146426-40-6; (kenpaullone) 142273-20-9; (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine) **212142-18-2**; (protein kinase C) 141436-78-4; (9 [(dimethylamino)methyl] 6,7,10,11 tetrahydro 9h,18h 5,21:12,17 dimethenodibenzo[e,k]pyrrolo[3,4 h][1,4,13]oxadiazacyclohexadecine 18,20(19h) dione) 169939-93-9, 169939-94-0; (olomoucine) 101622-51-9

CN Gleevec; Sti 571; Herceptin; **Cgp 79787**; **Ptk 787**; Ly 333531; Cgp 74514; Pkf 049 365

L101 ANSWER 3 OF 8 EMBASE on STN

AN 2002206850 EMBASE

TI Kinase insert domain-containing receptor kinase inhibitors as anti-angiogenic agents.

AU Bilodeau M.T.; Fraley M.E.; Hartman G.D.

CS G.D. Hartman, Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA 19486, United States

SO Expert Opinion on Investigational Drugs, (2002) 11/6 (737-745). Refs: 68
ISSN: 1354-3784 CODEN: EOIDER

CY United Kingdom

DT Journal; General Review

FS 005 General Pathology and Pathological Anatomy
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English

AB A variety of data accumulated during the past 10 years indicates that vascular endothelial growth factor-mediated angiogenesis is a key process in the growth of solid tumours. Efficacious and specific modulation of that signalling event through the inhibition of the cognate tyrosine kinase kinase insert domain-containing receptor (Flk-1) has been reported. A variety of small molecule kinase-domain-containing receptor kinase

inhibitors, including SU-5416, SU-6668, **PTK-787**, midostaurin, ZD4190 and ZD6474, have progressed to the clinical testing stage and this has allowed the direct and critical inspection of preclinical and clinical behaviour. The variety of potency, kinase selectivity and pharmacokinetic profiles offered by this group of compounds is providing important guidance for the efficacious use of these agents today and the design of second and third generation compounds for the future.

CT Medical Descriptors:
angiogenesis
tumor growth
solid tumor
signal transduction
drug efficacy
drug mechanism
drug research
drug potency
drug selectivity
drug use
drug design
drug clearance
drug formulation
drug structure
headache: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
phlebitis: SI, side effect
metabolic disorder: SI, side effect
advanced cancer: DT, drug therapy
fatigue: SI, side effect
diarrhea: SI, side effect
urine color
retina neovascularization: DT, drug therapy
drug blood level
rash: SI, side effect
hematologic disease: SI, side effect
liver toxicity: SI, side effect
hypertension: DT, drug therapy
human
nonhuman
mouse
rat
clinical trial
animal experiment
animal model
controlled study
review
Drug Descriptors:
*angiogenesis inhibitor: AE, adverse drug reaction
*angiogenesis inhibitor: CT, clinical trial
*angiogenesis inhibitor: AN, drug analysis
*angiogenesis inhibitor: CB, drug combination
*angiogenesis inhibitor: CR, drug concentration
*angiogenesis inhibitor: DV, drug development
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: PR, pharmaceutics
*angiogenesis inhibitor: PK, pharmacokinetics
*angiogenesis inhibitor: PD, pharmacology
*angiogenesis inhibitor: IP, intraperitoneal drug administration
*angiogenesis inhibitor: IV, intravenous drug administration
*angiogenesis inhibitor: PO, oral drug administration
vasculotropin inhibitor: AE, adverse drug reaction
vasculotropin inhibitor: CT, clinical trial

vasculotropin inhibitor: AN, drug analysis
vasculotropin inhibitor: CB, drug combination
vasculotropin inhibitor: CR, drug concentration
vasculotropin inhibitor: DV, drug development
vasculotropin inhibitor: DT, drug therapy
vasculotropin inhibitor: PR, pharmaceutics
vasculotropin inhibitor: PD, pharmacology
vasculotropin inhibitor: IP, intraperitoneal drug administration
vasculotropin inhibitor: PO, oral drug administration
protein tyrosine kinase inhibitor: AE, adverse drug reaction
protein tyrosine kinase inhibitor: AN, drug analysis
protein tyrosine kinase inhibitor: CB, drug combination
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: TO, drug toxicity
protein tyrosine kinase inhibitor: PK, pharmacokinetics
protein tyrosine kinase inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: PO, oral drug administration
zd 6474: AE, adverse drug reaction
zd 6474: AN, drug analysis
zd 6474: CB, drug combination
zd 6474: DV, drug development
zd 6474: DT, drug therapy
zd 6474: TO, drug toxicity
zd 6474: PD, pharmacology
zd 6474: PO, oral drug administration
pkc 412: CT, clinical trial
pkc 412: AN, drug analysis
pkc 412: DT, drug therapy
pkc 412: PK, pharmacokinetics
pkc 412: PD, pharmacology
pkc 412: PO, oral drug administration
midostaurin: CT, clinical trial
midostaurin: AN, drug analysis
midostaurin: DT, drug therapy
midostaurin: PK, pharmacokinetics
midostaurin: PD, pharmacology
midostaurin: PO, oral drug administration
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: AE, adverse drug reaction
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: AN, drug analysis
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CB, drug combination
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DV, drug development
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PR, pharmaceutics
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PK, pharmacokinetics
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: IP, intraperitoneal drug administration
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: IV, intravenous drug administration
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PO, oral drug administration
su 6668: AE, adverse drug reaction

su 6668: CT, clinical trial
su 6668: AN, drug analysis
su 6668: DT, drug therapy
su 6668: PR, pharmaceutics
su 6668: PK, pharmacokinetics
su 6668: PD, pharmacology
su 6668: IP, intraperitoneal drug administration
su 6668: IV, intravenous drug administration
su 6668: PO, oral drug administration
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: CT, clinical trial
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: AN, drug analysis
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: CB, drug combination
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DV, drug development
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: DT, drug therapy
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PK, pharmacokinetics
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PO, oral drug administration
staurosporine derivative: CT, clinical trial
staurosporine derivative: AN, drug analysis
staurosporine derivative: DT, drug therapy
staurosporine derivative: PK, pharmacokinetics
staurosporine derivative: PD, pharmacology
staurosporine derivative: PO, oral drug administration
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: AN, drug analysis
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: CR, drug concentration
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: DV, drug development
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: DT, drug therapy
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: PK, pharmacokinetics
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: PD, pharmacology
n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine: PO, oral drug administration
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
folinic acid: CT, clinical trial
folinic acid: CB, drug combination
folinic acid: DT, drug therapy
irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: DT, drug therapy
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
captopril: CB, drug combination
captopril: DT, drug therapy
zd 1839
vasculotropin: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound

aminotransferase: EC, endogenous compound
platelet derived growth factor: EC, endogenous compound
antihypertensive agent: CB, drug combination
antihypertensive agent: PD, pharmacology
unclassified drug

RN (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (su 6668) 252916-29-3; (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine) **212142-18-2**; (n (4 bromo 2 fluorophenyl) 6 methoxy 7 [2 (1h 1,2,3 triazol 1 yl)ethoxy] 4 quinazolinamine) 257938-36-6; (paclitaxel) 33069-62-4; (carboplatin) 41575-94-4; (doxorubicin) 23214-92-8, 25316-40-9; (fluorouracil) 51-21-8; (folinic acid) 58-05-9, 68538-85-2; (irinotecan) 100286-90-6; (gemcitabine) 103882-84-4; (captopril) 62571-86-2; (vasculotropin) 127464-60-2; (protein tyrosine kinase) 80449-02-1; (aminotransferase) 9031-66-7

CN (1) Su 5416; (2) Su 6668; **(3) Ptk 787**; (4) Zd 4190; (5) Zd 6474; (6) Zk 222584; (7) Pkc 412; (8) Zd 1839

CO (2) Sugen; (7) Novartis; (8) Astra Zeneca

L101 ANSWER 4 OF 8 EMBASE on STN

AN 2001305507 EMBASE

TI Angiogenesis factors.

AU Kuwano M.; Fukushi J.-I.; Okamoto M.; Nishie A.; Goto H.; Ishibashi T.; Ono M.

CS Dr. M. Kuwano, Department of Medical Biochemistry, Graduate School of Medical Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

SO Internal Medicine, (2001) 40/7 (565-572).
Refs: 57
ISSN: 0918-2918 CODEN: IEDIEP

CY Japan

DT Journal; General Review

FS 005 General Pathology and Pathological Anatomy
006 Internal Medicine
022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LA English

SL English

AB Angiogenesis is a recent highlight in the medical field; the developmental process and pathological conditions for various diseases can be understood from the novel aspect of "angiogenesis". Many angiogenesis-related factors are involved in the development of vessels during embryogenesis (vasculogenesis), as well as the induction of new vessels in response to physiological or pathological stimuli. In particular, the appearance of hemangioblasts, precursor cells for vascular endothelial cells and blood cells, and blood islands are expected to play a "prelude" role in tubulogenesis. Gene knock out mice of vascular endothelial growth factor (VEGF)/VEGF receptor, ephrin-B2, and angiopoietin-1 results in a failure of normal vessels production. Dormant factors derived from proteolytic cleavage of various physiological substrates are expected to balance a homeostasis of "angiogenic states" in the host. Furthermore, angiogenesis under various pathological conditions of malignant tumors, ocular diseases, psoriasis, rheumatoid arthritis, atherosclerosis and other diseases is associated with complex angiogenesis networks, suggesting pleiotropic mechanisms for angiogenesis.

CT Medical Descriptors:
*angiogenesis
cytokine production
embryo development
pathological anatomy
precursor cell

hemangioblast
drug targeting
vascular endothelium
knockout gene
protein degradation
cancer
eye disease
psoriasis
rheumatoid arthritis
atherosclerosis
disease association
human
nonhuman
mouse
clinical trial
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
meta analysis
human cell
review
Drug Descriptors:
*vasculotropin receptor: EC, endogenous compound
*ephrin: EC, endogenous compound
*ephrin b2: EC, endogenous compound
*angiogenic factor: EC, endogenous compound
*angiopoietin 1: EC, endogenous compound
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: PD, pharmacology
alpha interferon: CT, clinical trial
alpha interferon: PD, pharmacology
monoclonal antibody: CT, clinical trial
monoclonal antibody: PD, pharmacology
suramin: CT, clinical trial
suramin: PD, pharmacology
marimastat: CT, clinical trial
marimastat: PD, pharmacology
prinomastat: CT, clinical trial
prinomastat: PD, pharmacology
ae 941: CT, clinical trial
ae 941: PD, pharmacology
d 2163: CT, clinical trial
d 2163: PD, pharmacology
fumagillol chloroacetylcarbamate: CT, clinical trial
fumagillol chloroacetylcarbamate: PD, pharmacology
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
su 6668: CT, clinical trial
su 6668: PD, pharmacology
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: CT, clinical trial
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
zd 1839: CT, clinical trial
zd 1839: PD, pharmacology
monoclonal antibody 1m 609: CT, clinical trial
monoclonal antibody 1m 609: PD, pharmacology
cyclo(arginylglycyl alpha aspartyl dextro phenylalanyl n methylvalyl): CT, clinical trial
cyclo(arginylglycyl alpha aspartyl dextro phenylalanyl n methylvalyl): PD, pharmacology
combretastatin A4: CT, clinical trial
combretastatin A4: PD, pharmacology

endostatin: CT, clinical trial
endostatin: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: PD, pharmacology
unclassified drug
k 22584

RN (angiopoietin 1) 186270-49-5; (suramin) 129-46-4, 145-63-1; (marimastat) 154039-60-8; (prinomastat) 192329-42-3, 195008-93-6; (d 2163) 191537-76-5; (fumagillol chloroacetylcarbamate) 129298-91-5; (3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (su 6668) 252916-29-3; (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine) **212142-18-2**; (cyclo(arginylglycyl alpha aspartyl dextro phenylalanyl n methylvalyl)) 188968-51-6; (combretastatin A4) 117048-59-6; (endostatin) 187888-07-9; (thalidomide) 50-35-1

CN Ag 3340; Ae 941; Bms 275291; Tnp 470; Su 5416; Su 6668; **Ptk 787**; K 22584; Zd 1839; Vitaxin; Emd 121974

L101 ANSWER 5 OF 8 EMBASE
on STN

AN 2000403117 EMBASE

TI Selective tyrosine kinase inhibitors.

AU Wilkinson S.E.; Harris W.

CS W. Harris, Roche Discovery Welwyn, Roche Products Ltd., 40 Broadwater Road, Hertfordshire AL7 3AY, United Kingdom

SO Emerging Drugs, (2000) 5/3 (287-297).
Refs: 41
ISSN: 1361-9195 CODEN: EMDRFV

CY United Kingdom

DT Journal; General Review

FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English

AB The tyrosine specific protein kinases (TK) are a subgroup of the largest known gene family, the kinases. Latest estimates suggest that there are over 2000 kinases encoded in the human genome [1]. TKs catalyse the transfer of phosphate to the phenolic hydroxyl of tyrosine residues in substrate proteins, consequently modifying the target protein properties. By working in concert with tyrosine phosphatases, which drive the reverse process, the TKs provide a switching system resulting in the transduction of signals from cell surface receptor to the nucleus. Inappropriate activation of TKs can lead to abnormal, dysregulated cellular proliferation and many of the known oncogenes are kinases. Naturally, there has been great interest in TKs as potential molecular targets for developing drugs for the treatment of cancer and results from the first clinical trials are now being published. Preclinical research is also focused on other therapeutic applications of TK inhibitors. This review concentrates on TK inhibitors which are either already in the clinic or likely to enter Phase I studies in the near future.

CT Medical Descriptors:
*cancer: DT, drug therapy
drug structure
chronic myeloid leukemia: DT, drug therapy
acute lymphoblastic leukemia: DT, drug therapy
drug effect
drug mechanism
treatment outcome
lung non small cell cancer: DT, drug therapy
Kaposi sarcoma: DT, drug therapy
diabetic retinopathy: DT, drug therapy
angiogenesis

rheumatoid arthritis: DT, drug therapy
drug receptor binding
binding affinity
side effect: SI, side effect
human
nonhuman
clinical trial
review
Drug Descriptors:
*protein tyrosine kinase inhibitor: AE, adverse drug reaction
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: AN, drug analysis
*protein tyrosine kinase inhibitor: CM, drug comparison
*protein tyrosine kinase inhibitor: DV, drug development
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PK, pharmacokinetics
*protein tyrosine kinase inhibitor: PD, pharmacology
*protein tyrosine kinase inhibitor: PO, oral drug administration
vincristine: DT, drug therapy
taxol
taxotere
alendronic acid
pamidronic acid
rituximab
trastuzumab
zd 1839: AE, adverse drug reaction
zd 1839: CT, clinical trial
zd 1839: AN, drug analysis
zd 1839: CM, drug comparison
zd 1839: DT, drug therapy
zd 1839: PD, pharmacology
pd 0183805: CT, clinical trial
pd 0183805: AN, drug analysis
pd 0183805: DT, drug therapy
pd 0183805: PD, pharmacology
pd 0183805: PO, oral drug administration
pki 166: CT, clinical trial
pki 166: AN, drug analysis
pki 166: DT, drug therapy
pki 166: PD, pharmacology
4 (3 ethynylanilino) 6,7 bis(2 methoxyethoxy)quinazoline: CT, clinical trial
4 (3 ethynylanilino) 6,7 bis(2 methoxyethoxy)quinazoline: AN, drug analysis
4 (3 ethynylanilino) 6,7 bis(2 methoxyethoxy)quinazoline: CM, drug comparison
4 (3 ethynylanilino) 6,7 bis(2 methoxyethoxy)quinazoline: DT, drug therapy
4 (3 ethynylanilino) 6,7 bis(2 methoxyethoxy)quinazoline: PD, pharmacology
bibx 1382: CT, clinical trial
bibx 1382: DT, drug therapy
bibx 1382: PD, pharmacology
ptk 787: CT, clinical trial
ptk 787: AN, drug analysis
ptk 787: DT, drug therapy
ptk 787: PD, pharmacology
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: AN, drug analysis
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology

su 6668: CT, clinical trial
su 6668: AN, drug analysis
su 6668: DT, drug therapy
su 6668: PD, pharmacology
pd 166866: AN, drug analysis
pd 166866: DV, drug development
pd 166866: DT, drug therapy
pd 166866: PD, pharmacology
leflunomide: CT, clinical trial
leflunomide: AN, drug analysis
leflunomide: DT, drug therapy
leflunomide: PD, pharmacology
whi p 131: CM, drug comparison
whi p 131: PD, pharmacology
2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: AE, adverse drug reaction
2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: CT, clinical trial
2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: AN, drug analysis
2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: DT, drug therapy
2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: PD, pharmacology
ag 957: AN, drug analysis
ag 957: DV, drug development
ag 957: PD, pharmacology
whi p 154: AN, drug analysis
whi p 154: CM, drug comparison
whi p 154: DV, drug development
whi p 154: DT, drug therapy
whi p 154: PD, pharmacology
lfm a 13: AN, drug analysis
lfm a 13: DV, drug development
lfm a 13: PD, pharmacology
whi d 11: AN, drug analysis
whi d 11: DV, drug development
whi d 11: PD, pharmacology
pp 1: AN, drug analysis
pp 1: DV, drug development
pp 1: PD, pharmacology
pd 173956: AN, drug analysis
pd 173956: DV, drug development
pd 173956: PD, pharmacology
ct 5269: AN, drug analysis
ct 5269: DV, drug development
ct 5269: PD, pharmacology
rwj 64777: AN, drug analysis
rwj 64777: DV, drug development
rwj 64777: PD, pharmacology
ct 4694: AN, drug analysis
ct 4694: DV, drug development
ct 4694: PD, pharmacology
unindexed drug
unclassified drug
iressa
cgp 75166
cgp 79787
zk 22584
sti 571

RN (vincristine) 57-22-7; (taxol) 33069-62-4; (taxotere) 114977-28-5; (alendronic acid) 66376-36-1; (pamidronic acid) 40391-99-9, 57248-88-1; (rituximab) 174722-31-7; (trastuzumab) 180288-69-1; (4 (3 ethynylanilino)

6,7 bis(2 methoxyethoxy)quinazoline) 183319-69-9; (3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (leflunomide) 75706-12-6; (2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine) 152459-95-5

CN (1) Zd 1839; (2) Iressa; (3) Pd 0183805; (4) Pki 166; (5) Cgp 75166; (6) Cp 358774; (7) Bibx 1382; **(8) Ptk 787**; **(9) Cgp 79787**; (10) Zk 22584; (11) Su 5416; (12) Su 6668; (13) Pd 166866; (14) Su 101; (15) Arava; (16) Sti 571; (17) Ag 957; (18) Whi p 154; (19) Lfm a 13; (20) Whi d 11; (21) Pp 1; (22) Pd 173956; (23) Ct 5269; (24) Rwj 64777; (25) Ct 4694; (26) Whi p 131; Taxol; Taxotere; Fosamax; Aredia; Mabthera; Herceptin

CO (2) Astra Zeneca; (7) Boehringer Ingelheim; (15) Sugen; (16) Novartis; (17) National Cancer Institute; (21) Pfizer; (22) Warner Lambert; (24) RW Johnson; (25) Celltech; (26) Hughes institute

L101 ANSWER 6 OF 8 EMBASE on STN

AN 2000295707 EMBASE

TI Blockade of vascular endothelial cell growth factor receptor signaling is sufficient to completely prevent retinal neovascularization.

AU Ozaki H.; Seo M.-S.; Ozaki K.; Yamada H.; Yamada E.; Okamoto N.; Hofmann F.; Wood J.M.; Campochiaro P.A.

CS Dr. P.A. Campochiaro, Maumenee 719, Johns Hopkins Univ. Sch. of Med., 600 N. Wolfe Street, Baltimore, MD 21287-9277, United States. pcampo@jhmi.edu

SO American Journal of Pathology, (2000) 156/2 (697-707).
Refs: 25
ISSN: 0002-9440 CODEN: AJPAA4

CY United States

DT Journal; Article

FS 005 General Pathology and Pathological Anatomy
012 Ophthalmology
037 Drug Literature Index

LA English

SL English

AB Retinal vasculogenesis and ischemic retinopathies provide good model systems for study of vascular development and neovascularization (NV), respectively. Vascular endothelial cell growth factor (VEGF) has been implicated in the pathogenesis of retinal vasculogenesis and in the development of retinal NV in ischemic retinopathies. However, insulin-like growth factor-I and possibly other growth factors also participate in the development of retinal NV and intraocular injections of VEGF antagonists only partially inhibit retinal NV. One possible conclusion from these studies is that it is necessary to block other growth factors in addition to VEGF to achieve complete inhibition of retinal NV. We recently demonstrated that a partially selective kinase inhibitor, PKC412, that blocks phosphorylation by VEGF and platelet-derived growth factor (PDGF) receptors and several isoforms of protein kinase C (PKC), completely inhibits retinal NV. In this study, we have used three additional selective kinase inhibitors with different selectivity profiles to explore the signaling pathways involved in retinal NV.**PTK787**, a drug that blocks phosphorylation by VEGF and PDGF receptors, but not PKC, completely inhibited retinal NV in murine oxygen-induced ischemic retinopathy and partially inhibited retinal vascularization during development. CGP 57148 and CGP 53716, two drugs that block phosphorylation by PDGF receptors, but not VEGF receptors, had no significant effect on retinal NV. These data and our previously published study suggest that regardless of contributions by other growth factors, VEGF signaling plays a critical role in the pathogenesis of retinal NV. Inhibition of VEGF receptor kinase activity completely blocks retinal NV and is an excellent target for treatment of proliferative diabetic retinopathy and other ischemic retinopathies.

CT Medical Descriptors:
***retina neovascularization: ET, etiology**

***retina neovascularization: PC, prevention**
diabetic retinopathy: CO, complication
diabetic retinopathy: ET, etiology
retinopathy: CO, complication
retinopathy: ET, etiology
pathogenesis
signal transduction
eye blood flow
nonhuman
mouse
animal model
controlled study
animal tissue
newborn
article
priority journal
Drug Descriptors:
*vasculotropin
*vasculotropin receptor
*protein tyrosine kinase inhibitor: AD, drug administration
*protein tyrosine kinase inhibitor: CM, drug comparison
*protein tyrosine kinase inhibitor: DO, drug dose
*protein tyrosine kinase inhibitor: PD, pharmacology
*protein tyrosine kinase inhibitor: PO, oral drug administration
***ptk 787: AD, drug administration**
***ptk 787: DO, drug dose**
***ptk 787: PD, pharmacology**
***ptk 787: PO, oral drug administration**
*pkc 412: DO, drug dose
*pkc 412: PD, pharmacology
*2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: CM, drug comparison
*2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: DO, drug dose
*2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: PD, pharmacology
*n [4 methyl 3 [4 (3 pyridinyl) 2 pyrimidinylamino]phenyl]benzamide: CM, drug comparison
*n [4 methyl 3 [4 (3 pyridinyl) 2 pyrimidinylamino]phenyl]benzamide: DO, drug dose
*n [4 methyl 3 [4 (3 pyridinyl) 2 pyrimidinylamino]phenyl]benzamide: PD, pharmacology
platelet derived growth factor receptor
protein kinase C inhibitor
genistein
rhodopsin
unclassified drug
RN (vasculotropin) 127464-60-2; (2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine) 152459-95-5; (n [4 methyl 3 [4 (3 pyridinyl) 2 pyrimidinylamino]phenyl]benzamide) 152459-94-4; (genistein) 446-72-0; (rhodopsin) 60383-01-9, 9009-81-8
CN Cgp 57148; Cgp 53716; Pkc 412; **Ptk 787**

L101 ANSWER 7 OF 8 EMBASE
on STN
AN 2000267892 EMBASE
TI AE-941. Oncolytic antipsoriatic treatment of age-related macular degeneration angiogenesis inhibitor.
AU Sorbera L.A.; Castaner R.M.; Leeson P.A.
CS L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
SO Drugs of the Future, (2000) 25/6 (551-557).
Refs: 26
ISSN: 0377-8282 CODEN: DRFUD4

CY Spain
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Standardized shark cartilage liquid extract comprisins the 0-500 kDa molecular fraction.
CT Medical Descriptors:
*psoriasis
*cancer inhibition
***retina macula degeneration**
*angiogenesis
cartilage
drug mechanism
drug structure
shark
dose response
dose calculation
human
nonhuman
clinical trial
review
Drug Descriptors:
*neovastat: CT, clinical trial
*neovastat: AN, drug analysis
*neovastat: DV, drug development
*neovastat: DO, drug dose
*neovastat: TO, drug toxicity
*neovastat: PD, pharmacology
*ae 941: CT, clinical trial
*ae 941: AN, drug analysis
*ae 941: DV, drug development
*ae 941: DO, drug dose
*ae 941: TO, drug toxicity
*ae 941: PD, pharmacology
*angiogenesis inhibitor: CT, clinical trial
*angiogenesis inhibitor: AN, drug analysis
*angiogenesis inhibitor: DV, drug development
*angiogenesis inhibitor: DO, drug dose
*angiogenesis inhibitor: TO, drug toxicity
*angiogenesis inhibitor: PD, pharmacology
antipsoriasis agent: CT, clinical trial
antipsoriasis agent: AN, drug analysis
antipsoriasis agent: DV, drug development
antipsoriasis agent: DO, drug dose
antipsoriasis agent: TO, drug toxicity
antipsoriasis agent: PD, pharmacology
marimastat: CT, clinical trial
marimastat: PD, pharmacology
4 dedimethylaminosancycline: CT, clinical trial
4 dedimethylaminosancycline: PD, pharmacology
bms 275291: CT, clinical trial
bms 275291: PD, pharmacology
solimastat: CT, clinical trial
solimastat: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: PD, pharmacology
cdc 501: CT, clinical trial
cdc 501: PD, pharmacology
squalamine: CT, clinical trial
squalamine: PD, pharmacology
combrestatin a4 phosphate: CT, clinical trial

combrestatin a4 phosphate: PD, pharmacology
endostatin: CT, clinical trial
endostatin: PD, pharmacology
angiostatin: CT, clinical trial
angiostatin: PD, pharmacology
troponin I: CT, clinical trial
troponin I: PD, pharmacology
angiozyme: CT, clinical trial
angiozyme: PD, pharmacology
pi 88: CT, clinical trial
pi 88: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: PD, pharmacology
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
su 6668: CT, clinical trial
su 6668: PD, pharmacology
ptk 787: CT, clinical trial
ptk 787: PD, pharmacology
gfb 111: CT, clinical trial
gfb 111: PD, pharmacology
hyb 165: CT, clinical trial
hyb 165: PD, pharmacology
emd 121974: CT, clinical trial
emd 121974: PD, pharmacology
monoclonal antibody 1m 609: CT, clinical trial
monoclonal antibody 1m 609: PD, pharmacology
ro 317453: CT, clinical trial
ro 317453: PD, pharmacology
im 862: CT, clinical trial
im 862: PD, pharmacology
halofuginone: CT, clinical trial
halofuginone: PD, pharmacology
zd 6476: CT, clinical trial
zd 6476: PD, pharmacology
unindexed drug
unclassified drug
s 3304
fumagillol chloroacetylcarbamate
zd 6474

RN (marimastat) 154039-60-8; (4 dedimethylaminosancycline) 15866-90-7; (thalidomide) 50-35-1; (squalamine) 148717-90-2, 160022-48-0; (endostatin) 187888-07-9; (angiostatin) 172642-30-7, 86090-08-6; (troponin I) 77108-40-8; (3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (halofuginone) 55837-20-2, 64924-67-0, 7695-84-3; (fumagillol chloroacetylcarbamate) 129298-91-5

CN (1) Ae 941; (2) Neovastat; (3) Col 3; (4) S 3304; (5) Bb 3644; (6) Bms 275291; (7) Tnp 470; (8) Cdc 501; (9) Endostatin; (10) Angiostatin; (11) Angiozyme; (12) Pi 88; (13) Su 5416; (14) Su 6668; **(15) Ptk 787**; (16) Hyb 165; (17) Emd 121974; (18) Vitaxin; (19) Ro 317453; (20) Im 862; (21) Zd 6474; Gfb 111

CO (2) Aeterna; (3) Collagenex; (4) Shionogi; (5) Schering Plough; (6) Bristol Myers Squibb; (7) Takeda; (8) Celgene; (10) Entremed; (11) Ribozyme Pharmaceuticals; (12) Progen; (14) Sugen; (15) Novartis; (16) Hybridon; (17) Merck; (18) Applied Molecular Evolution; (19) Hoffmann La Roche; (20) Cytran; (21) Astra Zeneca; British Biotechnology; Chiron; Boston Life Sciences; Imclone; Magainin Pharmaceuticals; Oxigene; Collgard

L101 ANSWER 8 OF 8 EMBASE
on STN
AN 2000152769 EMBASE

TI Target molecules for anti-angiogenic therapy: From basic research to clinical trials.
AU Hagedorn M.; Bikfalvi A.
CS A. Bikfalvi, Laboratoire Facteurs de Croissance, Batiment Recherche Biologie Animale, Universite de Bordeaux I, Avenue des Facultes, 33405 Talence, France. a.bikfalvi@croissance.u-bordeaux.fr
SO Critical Reviews in Oncology/Hematology, (2000) 34/2 (89-110).
Refs: 222
ISSN: 1040-8428 CODEN: CCRHEC
PUI S 1040-8428(00)00056-1
CY Ireland
DT Journal; General Review
FS 012 Ophthalmology
016 Cancer
029 Clinical Biochemistry
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LA English
SL English
AB There is growing evidence that anti-angiogenic drugs will improve future therapies of diseases like cancer, rheumatoid arthritis and ocular neovascularisation. However, it is still uncertain which kind of substance, out of the large number of angiogenesis inhibitors, will prove to be a suitable agent to treat these human diseases. There are currently more than 30 angiogenesis inhibitors in clinical trials and a multitude of promising new candidates are under investigation in vitro and in animal models. Important therapeutic strategies are: suppression of activity of the major angiogenic regulators like vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF); inhibition of function of αv-integrins and matrix metalloproteinases (MMPs); the exploitation of endogenous anti-angiogenic molecules like angiostatin, endostatin or thrombospondin. Given the wide spectrum of diseases which could be treated by anti-angiogenic compounds, it is important for today's clinicians to understand their essential mode of action at a cellular and molecular level. Here we give an in-depth overview of the basic pathophysiological mechanisms underlying the different anti-angiogenic approaches used to date based on the most recent fundamental and clinical research data. The angiogenesis inhibitors in clinical trials are presented and promising future drug candidates are discussed. Copyright (C) 2000 Elsevier Science Ireland Ltd.
CT Medical Descriptors:
*angiogenesis
drug targeting
cancer: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
eye disease: DT, drug therapy
neovascularization (pathology): DT, drug therapy
pathophysiology
clinical research
endothelium cell
human
nonhuman
animal model
clinical trial
review
Drug Descriptors:
*angiogenesis inhibitor: PD, pharmacology
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: DV, drug development
*angiogenesis inhibitor: CT, clinical trial
*antineoplastic agent: PD, pharmacology

*antineoplastic agent: DT, drug therapy
*antineoplastic agent: DV, drug development
*antineoplastic agent: CT, clinical trial
vasculotropin: EC, endogenous compound
vasculotropin receptor: EC, endogenous compound
fibroblast growth factor: EC, endogenous compound
thrombocyte factor 4: EC, endogenous compound
angiogenin: EC, endogenous compound
cytokine: EC, endogenous compound
angiostatin: EC, endogenous compound
endostatin: EC, endogenous compound
thrombospondin: EC, endogenous compound
matrix metalloproteinase: EC, endogenous compound
integrin: EC, endogenous compound
plasminogen activator: EC, endogenous compound
plasminogen activator inhibitor: EC, endogenous compound
angiopoietin 1: EC, endogenous compound
angiopoietin 2: EC, endogenous compound
marimastat: PD, pharmacology
marimastat: CT, clinical trial
ag 3340: PD, pharmacology
ag 3340: CT, clinical trial
4 dedimethylaminosancycline: PD, pharmacology
4 dedimethylaminosancycline: CT, clinical trial
cgs 27023a: PD, pharmacology
cgs 27023a: CT, clinical trial
4 (4' chlorobiphenyl 4 yl) 4 oxo 2 (phenylthiomethyl)butyric acid: PD, pharmacology
4 (4' chlorobiphenyl 4 yl) 4 oxo 2 (phenylthiomethyl)butyric acid: CT, clinical trial
monoclonal antibody 1m 609: PD, pharmacology
monoclonal antibody 1m 609: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
leflunomide: PD, pharmacology
leflunomide: CT, clinical trial
flavopiridol: PD, pharmacology
flavopiridol: CT, clinical trial
fumagillol chloroacetylcarbamate: PD, pharmacology
fumagillol chloroacetylcarbamate: CT, clinical trial
cm 101: PD, pharmacology
cm 101: CT, clinical trial
combretastatin A4: PD, pharmacology
combretastatin A4: CT, clinical trial
squalamine: PD, pharmacology
squalamine: CT, clinical trial
taxol: PD, pharmacology
taxol: CT, clinical trial
interleukin 12: PD, pharmacology
interleukin 12: CT, clinical trial
alpha interferon: PD, pharmacology
alpha interferon: CT, clinical trial
metastat: PD, pharmacology
metastat: CT, clinical trial
bms 2752291: PD, pharmacology
bms 2752291: CT, clinical trial
ae 941: PD, pharmacology
ae 941: CT, clinical trial
neovastat: PD, pharmacology
neovastat: CT, clinical trial
emd 121974: PD, pharmacology

emd 121974: CT, clinical trial
rhumab anti vegf: PD, pharmacology
rhumab anti vegf: CT, clinical trial
ptk 787: PD, pharmacology
ptk 787: CT, clinical trial
zk 22584: PD, pharmacology
zk 22584: CT, clinical trial
angiozyme: PD, pharmacology
angiozyme: CT, clinical trial
purpurin: PD, pharmacology
purpurin: CT, clinical trial
suradista: PD, pharmacology
suradista: CT, clinical trial
thalidomid: PD, pharmacology
thalidomid: CT, clinical trial
zd 0101: PD, pharmacology
zd 0101: CT, clinical trial
carboxyamidoimidazole: PD, pharmacology
carboxyamidoimidazole: CT, clinical trial
ct 2584: PD, pharmacology
ct 2584: CT, clinical trial
im 862: PD, pharmacology
im 862: CT, clinical trial
benfluralin: PD, pharmacology
benfluralin: CT, clinical trial
unclassified drug

RN (vasculotropin) 127464-60-2; (fibroblast growth factor) 62031-54-3; (thrombocyte factor 4) 37270-94-3, 69670-74-2; (angiogenin) 97950-81-7; (angiostatin) 172642-30-7, 86090-08-6; (endostatin) 187888-07-9; (plasminogen activator) 9039-53-6; (plasminogen activator inhibitor) 105844-41-5; (angiopoietin 1) 186270-49-5; (angiopoietin 2) 194368-66-6; (marimastat) 154039-60-8; (ag 3340) 195008-93-6; (4 dedimethylaminosancycline) 15866-90-7; (cgs 27023a) 169799-04-6; (4 (4' chlorobiphenyl 4 yl) 4 oxo 2 (phenylthiomethyl)butyric acid) 179545-76-7, 179545-77-8; (3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (leflunomide) 75706-12-6; (flavopiridol) 146426-40-6; (fumagillol chloroacetylcarbamate) 129298-91-5; (cm 101) 188417-67-6; (combretastatin A4) 117048-59-6; (squalamine) 148717-90-2, 160022-48-0; (taxol) 33069-62-4; (interleukin 12) 138415-13-1; (purpurin) 81-54-9; (benfluralin) 1861-40-1

CN Ag 3340; Metastat; Cmt 3; Col 3; Bms 2752291; Ae 941; Neovastat; Cgs 27023a; Bay 12 9566; Rhumab anti vegf; Su 5416; **Ptk 787**; Zk 22584; Angiozyme; Su 101; Suradista; Purlytin; Tnp 470; Thalidomid; Zd 0101; Cm 101; Taxol; Ct 2584; Im 862; Benefin

=> d his

(FILE 'HOME' ENTERED AT 06:22:42 ON 13 OCT 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 06:23:01 ON 13 OCT 2004
L1 3220 S NC5/ES AND N2C4-C6/ES
L2 STR
L3 7 S L2
L4 658 S L2 FUL
SAV L4 FAY663/A
L5 STR L2
L6 18 S L5 CSS SAM SUB=L4
L7 333 S L5 CSS FUL SUB=L4
SAV L7 FAY663A/A
L8 325 S L4 NOT L7

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     FILE 'HCAOLD' ENTERED AT 06:27:44 ON 13 OCT 2004
L9             6 S L7
L10            4 S L8
L11            7 S L9,L10
                 SEL AN
                 EDIT /AN /OREF

     FILE 'HCAPLUS' ENTERED AT 06:28:35 ON 13 OCT 2004
L12           11 S E1-E7
                 SEL AN 3 5 9 11
L13            7 S L12 NOT E8-E15
L14          109 S L7
L15           52 S L8
L16          142 S L13-L15
L17            1 S US20040102444/PN OR (US2003-663464# OR YS2002-411669#)/AP,PRN
                 E CAMPOCHIARO P/AU
L18          120 S E3-E7
                 E WONG M/AU
L19          751 S E3-E38
                 E WONG MICHEL/AU
L20           33 S E4-E10
                 E YEN S/AU
L21          112 S E3,E8
L22           22 S E38-E41
                 E PA L17
                 E NOVARTI/PA,CS
L23         4463 S E5,E6 OR NOVARTIS?/PA,CS
L24           29 S L16 AND L17-L23
                 E EYE/CT
L25        64373 S E3-E151
                 E E3+ALL
L26        75310 S E8,E7+NT
                 E E25+ALL
L27        32125 S E8,E9,E7+NT
                 E EYE DISEASE/CT
L28         9912 S E23
L29        24019 S E24-E108
L30         4005 S E109-E115
L31         8855 S E133,E136-E141
                 E EYE+ALL/CT
                 E E26+ALL
L32        12626 S E11,E12,E10+NT
                 E E38+ALL
L33         4225 S E4,E3+NT
L34         1383 S E16+OLD,NT OR E15+OLD,NT
                 E EYE+ALL/CT
                 E E27+ALL
L35         3320 S E4,E5,E3+NT OR E10+OLD,NT
L36       121715 S EYE OR ?OCULAR? OR ?OPHTHALM?
L37       113531 S EYE?
L38        51022 S ?RETINA OR ?RETINAL OR ?RETINAS OR ?RETINOPATH? OR MACUL?(L)D
L39            9 S L24 AND L25-L38
L40            6 S L39 AND ?DIABET?
L41            9 S L39,L40
L42           23 S L16 AND L25-L38
L43           16 S L42 AND ?DIABET?
L44           23 S L42,L43,L41
L45           19 S L44 AND (PD<=20020918 OR PRD<=20020918 OR AD<=20020918)
L46            7 S L45 AND L24
L47           12 S L45 NOT L46
                 SEL DN AN 1 10 11
L48            9 S L47 NOT E1-E9
L49           16 S L46,L48
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L50           4 S L44 NOT L45
L51           1 S L50 AND OCULAR THERAPY
L52          17 S L49,L51
L53          17 S L17,L52 AND L12-L52
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 06:49:35 ON 13 OCT 2004
L54          38 S E10-E47
L55           5 S L54 AND ?PIPER?/CNS
L56           5 S L54 AND 46.156.1/RID
L57          33 S L54 NOT L55,L56
L58           6 S L57 AND (C23H25N3O OR C24H27N3O OR C23H24CLN3O OR C23H24FN3O
L59          27 S L57 NOT L58

     FILE 'HCAPLUS' ENTERED AT 06:55:08 ON 13 OCT 2004
L60          90 S L59
L61          81 S VATALANIB? OR PTK787 OR PTK 787 OR PTKZK OR PTK ZK OR CGP7978
L62         108 S L60,L61
L63          69 S L62 AND (PD<=20020918 OR PRD<=20020918 OR AD<=20020918)
L64          26 S L63 AND L17-L23
L65          21 S L63 AND L25-L38
L66          14 S L64,L65 AND ?DIABET?
L67           9 S L64 AND L65,L66
L68          21 S L65-L67
L69          17 S L64 NOT L65,L66
L70           6 S L68 NOT EYE?/CW
L71           1 S L70 AND RETINA
L72           2 S L51,L71
L73          15 S L68 NOT L70
L74           2 S L73 NOT L53
L75           1 S L74 NOT MELANOMA
L76          13 S L73 NOT L74
L77          16 S L72,L75,L76
L78           2 S L77 AND DIABET?/CT
L79          12 S L77 AND ?ANGIOGEN?
L80          16 S L77-L79

     FILE 'REGISTRY' ENTERED AT 07:05:50 ON 13 OCT 2004

     FILE 'HCAPLUS' ENTERED AT 07:05:58 ON 13 OCT 2004

     FILE 'BIOSIS' ENTERED AT 07:08:47 ON 13 OCT 2004
L81          82 S L59 OR L61
L82          43 S L81 AND PY<=2002
L83           6 S L82 AND L36-L38
                SEL DN AN 6
L84           1 S E48-E49 AND L83
L85           2 S L82 AND (20006 OR 20004)/CC
L86           1 S L82 AND MACUL?(L)(DEGEN? OR OEDEM? OR EDEM?)
L87           2 S L82 AND ?RETINOPATH?
L88           2 S L84-L87
L89           2 S L82 AND (EYE+NT OR EYE DISEASE+NT)/CT
L90           2 S L88,L89

     FILE 'BIOSIS' ENTERED AT 07:14:43 ON 13 OCT 2004

     FILE 'MEDLINE' ENTERED AT 07:15:00 ON 13 OCT 2004
L91          67 S L59 OR L61
L92          26 S L91 AND PY<=2002
L93           1 S L92 AND (EYE+NT OR EYE DISEASES+NT)/CT
L94          25 S L92 NOT L93
L95          20 S L92 AND L38
L96           1 S L94 AND RETIN?
```

```
L97             2 S L93,L96

     FILE 'MEDLINE' ENTERED AT 07:17:10 ON 13 OCT 2004

     FILE 'EMBASE' ENTERED AT 07:17:32 ON 13 OCT 2004
L98           316 S L59 OR L61
L99           115 S L98 AND PY<=2002
                  E EYE/CT
L100            0 S L99 AND E3+NT,PFT,RT
                  E EYE DISEASE/CT
L101            8 S L99 AND E3+NT,PFT,RT

     FILE 'EMBASE' ENTERED AT 07:19:17 ON 13 OCT 2004

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